

T H E S I S
presented for the DEGREE of DOCTOR of MEDICINE,
UNIVERSITY of EDINBURGH,
BY
THOMAS CARLYLE MITCHELL, M.B., Ch.B., (Edin.)

THE SIGNIFICANCE of VARIATION in CONCENTRATION
OF CHLORIDES, ACID, and PEPSIN, in the
GASTRIC CONTENTS,
WITH PARTICULAR REFERENCE to the CONTROL of
GASTRIC ACIDITY.

September, 1929.



T A B L E o f C O N T E N T S .

	PAGE
Introduction	1.
Materials and Methods	17.
Resumé of Results	27.
Discussion of Results	28
Pepsin Variations	59
(a) Introduction & Description of Pepsin-methods	61.
(b) Pepsin Charts	
1. Experimental Charts	
2. Clinical Charts.	
(c) Discussion of Pepsin Results	67.
Summary & Conclusions	72
Bibliography	I.-VII.
One Hundred Clinical Charts. (without pepsin)	
Appendix	74-81.
Experimental Charts.	
Diagrams of Operations	
Photographs.	

THE SIGNIFICANCE of VARIATION in CONCENTRATION
of CHLORIDES, ACID, and PEPSIN, in the
GASTRIC CONTENTS,
WITH PARTICULAR REFERENCE to the CONTROL of
GASTRIC ACIDITY.

During digestion in the normal stomach, the concentration of chlorides, acid and pepsin, respectively, in the gastric contents, varies from time to time. The following study is an attempt to find the true significance of these variations; the chemical changes in food-material brought about by digestion, are not dealt with.

The object of this investigation is the explanation of the various concentration-curves of chlorides, acid and pepsin, during gastric digestion. Both normal and pathological cases have been studied, the latter principally in so far as they represent the behaviour of the normal functions under abnormal conditions. Where, however, the results indicate a means of attaining greater accuracy in the diagnosis of disease, attention has been drawn to this.

The regulation of the acidity of the gastric contents has, of late, provoked much speculation and discussion. This is an important part of the/

the main problem and is discussed with it. A full knowledge of the way in which gastric acidity is controlled will throw light upon the series of disorders in which abnormal acid-variations form a prominent feature.

It has been found convenient to treat the pepsin-variation in a separate section.

The presence of an acid in the stomach was known to physiologists in the eighteenth century. In 1752, REAUMUR⁽⁵⁷⁾, administered food, in perforated metal capsules and tubes, to birds, which were destroyed shortly afterwards. A markedly acid reaction was found in the contents of the capsule, and in the juice expressed from the mucous membrane. These experiments were repeated in many animals by SPALLANZI⁽⁷¹⁾, who confirmed the findings of acid.

It was for many years believed that this was due to lactic acid produced by food-fermentation, and it remained for PROUT⁽⁵⁶⁾, in 1824, to prove that hydrochloric acid was responsible for the acidity of the contents of the stomach.

From this time until as late as 1879, the acidity of the gastric juice was generally believed to be from 0.1 to 0.2% 'free' hydrochloric acid, approximately = 30 to 60 cc.N/10 sodium hydroxide per 100 cc., and when an acidity above the latter figure was found, this was taken as indicating 'hyperacidity' of the secretion.

When/

When HEIDENHAIN⁽³²⁾, in that year succeeded in obtaining pure juice from an isolated pouch in the fundus of the dog's stomach, the finding of an acidity of 0.45% hydrochloric acid (= 125 cc.N/10 NaOH), in the secretion obtained, led him, at first, to suppose that an error in titration had been made, but this impression was speedily corrected.

HEIDENHAIN then realised that the comparatively low figures, previously given for acidity of the secretion, resulted from failure to distinguish between gastric juice and gastric contents, that is, the juice mixed with other substances present in the stomach at the same time.

KAMENSKY⁽³⁷⁾, and RIA NTZEFF⁽⁵⁹⁾, found a corresponding high acidity of the pure gastric juice in rabbits and cats, respectively, and further support was given by the classical researches of PAVLOV⁽⁵³⁾ upon dogs' stomachs. This worker, observing that the operation of HEIDENHAIN necessitated division of the nerves coursing in the wall of the stomach, set about devising a method which, while retaining the advantages of the HEIDENHAIN pouch, might still preserve the nervous distribution. The result was the well-known "Pavlov-pouch", the formation of which will be described later. (Appendix p. 79)

PAVLOV/

PAVLOV was strongly of opinion that the gastric juice, in its freshly-secreted state, had a constant acidity. BEAUMONT⁽³⁾, in his observations upon Alexis St.Martin, a French-Canadian soldier with a permanent gastric fistula the result of a gunshot wound, first realised that the gastric mucous membrane, in its resting state, was slightly alkaline. PAVLOV noted that the first scanty portions of secretion from a pouch were less acid than those succeeding and attributed this fact to the neutralising effect of the alkaline mucus.

He explained the comparatively low acidity of the first part of the secretion by assuming that this flowed slowly over a considerable area of mucous membrane covered with mucus. As secretion became accelerated, the juice did not remain for so long a time in contact with the mucosa and was, therefore, neutralised to a less extent. In addition, the continued secretion had the mechanical effect of removing mucus, so that the late samples were not neutralised to the same degree as the early specimens, although the rate of flow was no greater.

PAVLOV suggested that neutralisation by alkaline mucus might be a protective function designed to prevent excessive acidity.

It/

It is known that during digestion, the acidity of the gastric contents usually attains the level most suitable for peptic digestion, viz:- 0.1 - 0.2% 'free' hydrochloric acid. As this is brought about by the continuous addition of secreted hydrochloric acid to the contents, the acidity tends, after a time, to rise above this 'optimum'-level and, on leaving the stomach, to irritate the mucous membrane of the small intestine.

In the majority of normal cases it is found that the acidity rarely exceeds the optimum to any considerable degree; there must exist, therefore, some controlling mechanism.

To explain this there are three principal theories, given below.

- (1) As the concentration of acid in the stomach tends to rise above the optimum-level, there occurs regurgitation of alkaline duodenal material through the pylorus into the stomach, and consequent reduction in the acidity of its contents.
- (2) During the first 'phase' of gastric secretion in response to food, the freshly-secreted juice is strongly acid; when the optimum is attained the acidity of the juice diminishes - the second 'phase'.

(3)/

- (3) The mucous membrane of the pyloric antrum of the stomach provides an alkaline secretion which neutralises the excess of acid.
-

(I). The occasional presence of bile in the stomach was first noted by BEAUMONT⁽³⁾, in 1824, but its significance was not seriously considered until discussed in 1907 by BOLDIREV⁽⁶⁾, who saw that it was necessary to discriminate between contents of the stomach alone, and contents of the stomach mixed with intestinal secretions. He showed that the introduction of oil into the stomach was followed by the appearance therein of bile. As in the case of oil, 0.5% hydrochloric acid was found by BOLDIREV to provoke the regurgitation of duodenal contents, and in so doing was reduced in concentration to approximately 0.15% 'free' hydrochloric acid. Presumably, this reduction was due to alkali in the regurgitated material. In 1914⁽⁷⁾, he published the results of his researches on dogs, in which he demonstrated that, of all available neutralising agents, by far the most powerful was the alkali of the pancreatic secretion, sodium carbonate.

He/

He put forward the interesting view that neutralisation of excessive acid, by regurgitation of alkaline duodenal contents, formed the normal control of gastric acidity. If, on the other hand, weakly-acid, neutral, or alkaline solutions were introduced into the stomach, the same optimum concentration was secured by the addition to the contents of secreted hydrochloric acid.

The whole process was named by him the "Self-Regulation of the Acidity of the Gastric Contents".

BOLDIREV believed that strongly-acid gastric contents, after passage through the pylorus, provoked antiperistaltic movements in the duodenum. Together with rejection there was regurgitation of neutralising alkali sufficient to render the contents non-irritating to the duodenum. When this was attained the stomach was permitted to empty.

His views were shared by MIGAI and CARLSON, (58) (14)
 SON, (quoted by REHFUSS, ,p.283), CATHCART ,
 and others.

REHFUSS (72) , working with the routine fractional method in man introduced by him in 1914, found trypsin, believed to be regurgitated from the duodenum, in easily-detectable amounts, in the resting and digesting/

digesting stomach. The values for trypsin were roughly inversely proportional to the acidity.

Further support was given, in 1922, by BOLTON & GOODHART⁽⁹⁾, who included estimations of total and mineral chlorides in the routine fractional gastric analysis in man. These workers concluded that the fall in acidity, with a rise in concentration of neutral chloride, towards the close of digestion, was convincing proof of neutralisation of hydrochloric acid by the alkali of the pancreatic secretion.

They stated that the total chlorides curve represented the true secretory curve of the stomach, and that the curve of neutral chloride represented the degree of neutralisation at various stages.

They believed that the rise of the total chlorides curve was undoubtedly due to the addition to the stomach contents of hydrochloric acid, and that at a given time during digestion, the pylorus relaxed, permitting duodenal reflux, producing a fall in the acidity of the gastric contents, and a coincident rise in the concentration of neutral chloride. They further maintained that a 'climbing' hydrochloric acid curve was due to insufficient regurgitation from the duodenum and that achlorhydria, or absence/

absence of 'free' hydrochloric acid, in the presence of normal values for total chlorides, was an indication that excessive regurgitation had occurred.

(11)
BOLTON & SALMOND, examined 100 normal cases for radiological demonstration of regurgitation; a returning stream of barium was distinctly seen in six cases only. More often a 'duodenal-cap' distended with the opaque emulsion, was observed to empty simultaneously with relaxation of the pyloric sphincter; presumably this indicated reflux of the meal into the stomach from the first part of the duodenum.

(II) Recently BOLDIREV'S view has been rejected by some observers. These consider that the neutral chloride of the stomach contents is, in normal cases not produced by the interaction of hydrochloric acid and alkali, but is actually secreted by the gastric glands.

According to this theory, the acidity of the secretion varies, but the concentration of total chlorides remains fairly constant; because the total chlorides comprise the sum of the acidity and neutral chloride, these last two vary in inverse proportion.

They hold that the acidity of the first part of the secretion is high, and its neutral chloride/

chloride concentration low; as the optimum acidity for peptic digestion is approached, the concentration of the neutral chloride begins to increase at the expense of that of the acid. Thus the replacement of a highly acid secretion by one rich in neutral chloride, prevents the gastric contents from exceeding the optimum of acid-concentration.

The idea of a diluting secretion of this nature is by no means a new one. MEADE-SMITH⁽⁷⁰⁾, ROTH & STRAUSS⁽⁶⁵⁾, and VON MERING⁽⁴⁷⁾, towards the close of the last century were of opinion that alteration in chemical composition of the gastric contents was due to three factors;

- (a) diffusion and osmosis through the stomach wall,
- (b) the addition to the gastric contents of the specific secretion, namely hydrochloric acid and pepsin, and
- (c) 'verdunnungsftsekretion', a diluent poured out by the glands.

In 1901, JUSTESEN⁽³⁶⁾, employing fractional gastric analysis, found that the curves of total chlorides and of acid, ran parallel in the earlier stages of gastric digestion, to diverge later, when the acid curve fell. He believed that the reduction of acidity was due to dilution by diffusion into the stomach/

stomach contents of sodium chloride from the blood. The curve of total chlorides would be relatively less affected by this chloride-containing diluent.

A few years later ROSEMAN⁽⁶²⁾, working with the preparation in dogs of the whole stomach and employing the method of 'sham-feeding', noted, in addition to the relatively low figures for acid obtained at the beginning of the outpouring of the juice, a fall in acidity at the time when digestion would normally be coming to a close. In 1920,⁽⁶³⁾ he advanced the view that while the total chlorides concentration of the juice remained constant, its acidity varied in direct proportion with the strength of the stimulus received by the gastric cells, in other words, according to the requirements of digestion.

HANSMAN, DAY & CLIFTON⁽²⁸⁾, have suggested the 'passage' through, - not necessarily the 'secretion' by - the stomach-wall of neutral chloride.

MORRELL ROBERTS⁽⁶⁰⁾, while investigating the action of atropine in inhibiting hydrochloric acid secretion, came to the conclusion that a fixed proportion of the total chloride of the juice is secreted in its neutral form, and that the remainder is potentially capable of being transformed into hydrochloric acid, the unaltered portion being secreted as such.

HEILMEYER⁽³²⁾, is of opinion that while the 'parietal' cells of the gastric mucosa secrete hydrochloric acid, the 'central' cells are responsible for the production of neutral chloride.

Recently, MACLEAN⁽⁴³⁾, has published results obtained from dogs, with a 'Pavlov-pouch', in which the curves of acid, of total and of mineral chlorides resemble those of the human normal fractional analysis in which allowance has been made for the factor of dilution by the test-meal.

In a later communication⁽⁴⁴⁾, he states that acid solutions introduced into the stomach of man, are reduced in acidity by the secretion of a juice rich in neutral chloride, and that solutions of sodium chloride call forth an acid secretion, the final result being similar, namely, the production of an acidity of the gastric contents of 0.1 - 0.2% hydrochloric acid, the optimum, as pointed out by BOLDIREV, for peptic-digestion, but non-irritant to the duodenal mucous membrane.

(III.) The third view that there is neutralisation of excessive acid by the alkaline secretion of the pylorus, described by KLEMENSIEWICZ⁽³⁸⁾, and confirmed by HEIDENHAIN⁽³⁰⁾, and ACKERMANN⁽¹⁾ was first put forward by PFAÜNDLER⁽⁵⁴⁾, in 1900.

Recent/

Recent supporters of this view are BAIRD
(2)
CAMPBELL & HERN ,who demonstrated, in one case,
reduction of acidity although regurgitation had been
prevented by applying continuous suction to the duo-
denum.

Up to the present time, very little inte-
rest has been exhibited in this explanation of gas-
tric acidity-control, owing partly, no doubt, to
the technical difficulties of obtaining direct evi-
dence as to the behaviour of the pyloric segment
when not isolated from the rest of the stomach.

At/

At the outset, the object of investigation was to determine, if possible, the diagnostic value of a fuller examination of gastric contents than is the custom.

Shortly after the commencement of the study there appeared, in one of the medical weekly journals, much correspondence on the subject of the gastric secretion of neutral chloride.

Thereafter, the research tended to proceed along the lines of an inquiry into gastric physiology, particularly regarding the function of acidity-control in both normal and pathological cases. Animal-experimentation was undertaken for the purpose of more closely inquiring into certain problems that arose during the clinical studies.

In a number of cases, pepsin was estimated in the fractional samples by a method recently introduced by Dr. W. O. Kermack of the Laboratory of the Royal College of Physicians, Edinburgh. This is described in the separate section previously alluded to.

The/

The research extended over the period : -
April 1928 to July 1929.

Clinical study was undertaken in the wards of the Chalmers Hospital, and of the Royal Infirmary, Edinburgh.

Laboratory estimations were carried out by the author in the Chalmers Hospital, the Department of Biochemistry of the Royal Infirmary, and the Laboratory of the Royal College of Physicians, Edinburgh.

Animal experiments were performed in the Department for Surgical Research of the University of Edinburgh.

The writer wishes to acknowledge his indebtedness to Dr.A.Fergus HEWAT, and Mr J.W. DOWDEN of the consultant staff of the Chalmers Hospital, and to the physicians and surgeons of the Royal Infirmary, for the use of clinical material in the wards under their charge; to Professor D.P.D. WILKIE, Professor D. MURRAY LYON, and Colonel G. McKENDRICK for permission to work in the departments under their supervision, and to Dr. W.O. KERMAK for much helpful advice, and for kind permission to make use of the method devised by him for the quantitative determination of pepsin.

FINALLY/

Finally, acknowledgments are due to those graduates, undergraduates and others who volunteered for the normal series of observations, and to the staffs of the various wards and laboratories for their helpful co-operation.

MATERIALS/

MATERIALS AND METHODS.

After complete removal of the fasting-juice, an ordinary 'gruel-meal' was administered, specimens of gastric contents being thereafter obtained every quarter of an hour for a period of two hours. The actual technique differed in no essential particulars from that usually employed and need not be described here.

Two points, however, received special attention, first no salt was added to the oatmeal gruel, and second, when once the Ryle's tube was in position, precautions were taken that saliva should not be swallowed, a receptacle for this being provided.

When the specimens were not to be investigated within a few hours, they were stored in a refrigerator, particularly where estimations of pepsin were contemplated. Prior to analysis, filtration or centrifugation of the specimens was done, when necessary.

Samples were examined for the presence of the following constituents: Mucus, Bile, Blood and Starch. The amounts of these were judged visually and represented as Tr. (= Trace) +, ++, +++. When absent, no sign was written. Blood was not tested for/

for in every specimen, but where there was reason to suspect its presence, the following test (4) was performed: -

The residue from filtration is boiled in 3 c.c. of distilled water and then cooled under the tap. Two drops of acetic acid and 4 cc. of ether are added; the tube is inverted several times, shaking being avoided.

Two similar test tubes are prepared as follows: -

Into each are placed 3 c.c. of hydrogen peroxide and 3 c.c. of tincture of guaiacum. To one tube the ethereal extract is added: if blood be present, a deep blue colour develops, contrasting with the light brown of the control.

LACTIC ACID: MACLEAN'S test ⁽⁴⁴⁾, was not found suitable as the 5% solution of ferric chloride frequently precipitated the protein of the contents and obscured the reactions; also, the presence of bile interfered with the detection of the colour signifying a positive result.

An attempt was made to find a suitable precipitant of protein, so that the ferric chloride solution might be brought into contact with a protein-free filtrate. No satisfactory reagent was found and this line of investigation was abandoned.

The/

The best results were finally obtained by the following methods: -

An ethereal extract of the contents is added to one of two tubes each containing 2 drops of 5% aqueous solution of ferric chloride in 5 c.c. of distilled water. Where lactic acid is present, a canary-yellow colour develops at the interface of the two fluids, and diffuses downwards throughout the solution. This test is a modification of that associated with the name of Strauss.

A N A L Y S I S .

The method employed for estimating total chlorides was that published by PATTERSON⁽⁵²⁾. Its principle depends on the fact that the disturbing effect of the protein in gastric contents, upon the interaction of chloride and silver nitrate, can be overcome by the presence of an excess of nitric acid. The advantages of the method are, that it is fairly rapidly and easily carried out and that only a small volume of contents is required.

T E C H N I Q U E .

4 c.c. of acetone are placed in a porcelain basin, and 3 c.c. of nitric acid are run in from a burette; the acetone forms a layer above the nitric acid/

acid and prevents the fuming of the latter. 0.2 c.c. of the stomach contents are taken in a special pipette and blown into the nitric acid, acid being used to wash out the pipette. The acid is removed by rinsing with acetone, and the pipette is then dried. A glass rod is used to mix the gastric contents and nitric acid. 1 c.c. of an N/30 aqueous solution of silver nitrate is next run into the basin, and the mixture again stirred. Two drops of a saturated aqueous solution of iron alum are then added. N/30 ammonium thiocyanate solution (prepared by diluting one part of N/10 aqueous solution of ammonium thiocyanate with two parts of absolute alcohol) is then run in from a special micro-burette, graduated in hundredths of a c.c., until the first permanent trace of pink colour is obtained, stirring being kept up continuously. The chloride value, in terms of c.c. of N/10 NaOH per 100 c.c. of contents is then given by the formula $(1 - x) \times \frac{100}{0.2} \times \frac{1}{3}$, where 'x' is the number of c.c. of thiocyanate required in the titration. A table was constructed to give, at a glance, the results of this formula for each reading of the burette.

The/

The chloride content of the meal is stated by BOLTON⁽¹⁰⁾, to be very small. A trial of the above method on carefully standardised N/10 HCl, enables a correction to be applied to the results obtained from gastric samples. This is required in order to compensate for inaccuracies in the graduating of apparatus and in the preparation of standard solutions.

The concentrations of free and total acid in the contents, expressed in terms of c.c. of NaOH, N/10, were estimated by the routine method of titration with N/10 alkali, using as indicators methyl orange and phenolphthalein, respectively. It was found convenient to take small quantities of stomach contents - 2 c.c. - and run in alkali from the micro-burette. The presence of free hydrochloric acid was confirmed by GÜNZBERG'S test. Neutral chloride was estimated by deducting the figures obtained for total acidity from those of the total chlorides. PATTERSON points out that this is sufficiently accurate unless large amounts of lactic acid are present in the stomach contents.

RESULTS/

R E S U L T S .

The cases investigated comprise:-

- a) Persons believed to be normal as regards the gastric functions, and as nearly as possible normal in other respects.
- b) Persons in whom some pathological process, whether of the alimentary or other systems was demonstrated or suspected.

For the purposes of this paper, results were, as far as practicable, selected from cases in which the diagnosis was established either by operation or by accepted clinical tests.

Detailed results of investigations will be found in the form of special charts at the end of the thesis.

Cases have been divided into groups according to the anatomical system involved, the organ affected and the pathological process. A miscellaneous group has been formed containing not more than two cases of any one disease, irrespective of the system implicated.

Each group has been given an index letter or letters, as follows:-

NORMALS/

NORMALS	= N	(10 Cases; 10 Investigations).		
CHRONIC GASTRIC ULCER	= UV	8	do. 13	do.
CARCINOMA of STOMACH	= CV	3	do. 3	do.
CHRONIC PRIMARY GASTRITIS	= G	3	do. 4	do.
CHRONIC DUO- DENAL ULCER	= DU	11	do. 18	do.
CHOLELITHI- ASIS	= VC	6	do. 6	do.
CHRONIC AP- PENDICITIS	= AV	11	do. 12	do.
PERNICIOUS ANAEMIA	= PA	3	do. 3	do.
FUNCTIONAL	= IF	16	do. 16	do.
MISCELLANE- OUS	= M	15	do. 15	do.
<hr/>				
86 CASES 100 INVESTIGATIONS.				

In order to facilitate a comprehensive survey of the results, certain features have been selected and arranged in order as follows:-

1./

1. Number of investigations made.
2. In the curve of total chlorides -
 - a) the fasting level,
 - b) the highest figure attained after ingestion of the meal, and
 - c) number of the specimen in which this occurred.
3. In curve of total acidity -

the same three points as in the curve of total chlorides.
4. In curve of mineral chloride -
 - a) the fasting level,
 - b) the level at the end of the period of observation, i.e. two hours after ingestion of the meal.
5. MUCUS - percentage of total number of specimens in which this was present.
6. BILE - percentage, as for mucus.
7. BLOOD - percentage, as for mucus.
8. STARCH - number of the specimen in which this was last observed.
9. ACHLORHYDRIA - percentage of group-investigations in which 'free' hydrochloric acid was absent throughout the test.

Where possible, figures are given as a mean with standard deviations; the latter is calculated by the method described by HALBERT L. DUNN⁽¹⁷⁾, of taking the square root of the sum of the squared differences between the mean and its components.

The/

The mean, plus or minus two standard deviations, includes 95% of cases in the series examined.

The occurrence of certain constituents, such as mucus, blood, etc., has been recorded in percentages.

The difference between the means of two groups is 'significant' when it is unlikely that such a difference could have arisen in the combined variation-ranges of components in both groups. The likelihood of this occurrence is determined by the application of the following formula, quoted by
(20)
FISHER :-

F O R M U L A .

\bar{x}_1 = mean of group 1 of $n_1 + 1$ samples.

\bar{x}_2 = " " group 2 of $n_2 + 1$ samples.

$$s^2 = \frac{s_1^2 (n_1 + 1) + s_2^2 (n_2 + 1)}{n_1 + n_2 + 2}$$

$$t = \frac{\bar{x}_1 - \bar{x}_2}{s} \sqrt{\frac{(n_1 + 1)(n_2 + 1)}{n_1 + n_2 + 2}}$$

$$n = n_1 + n_2$$

s = sum of squared differences from mean.

't' is obtained from a table for the particular of 'n'

A significant difference is one where the chances of its arising as a sampling variation, are less than 5 in 100.

The value of these statistical methods in reviewing data is incontestable.

TABLE/

TABLE of MEANS.

STANDARD DEVIATIONS and PERCENTAGES in VARIOUS GROUPS.

CASE	NO.	F.J. C.C.	Cl.		HCl.		NaCl.		M	B	BL	ST.	A
			F	H	TB	F	H	TB	F	TL	%	%	%
N M	10	32	91	103	6	33	63	5	59	47	20	26	0
SD		22.2 496	18.2 335	22.9 510	1.8	18.9 356	21.0 441		10.9 119	18.9 359		1.6	
A UV M	8	48	110	108	6	37	65	5	73	56	28	11	0
SD		33.8 1112	21.8 477	8.3 72	2.4	16.2 263	15.0 227	1.4	14.7 217	10.3 111		1.0	
B UV M	5	29	100	114	6	24	37	3	77	85	17	50	0
SD		15.3 236	37.8 1404	17.8 315	1.8	17.2 297	16.2 262	2.0	14.9 1500	11.2 129		1.0	
CV M	3	35	81	80	8	23	29	6	57	56	98	4	100
SD		17.0 287	9.3 89	13 170	0	4.1 17	8.4 70	1.1	9.8 97	25.7 659			
G M	3	20	65	66	7	10	14	4	54	51	83	4	100
SD		8.1 67	18.8 356	12.7 156	.2	1.3 1.7	6.8 46	1.6	18.2 339	2.0 4		.2	

A	10	40	111	112	6	53	73	5	58	57	13	30	2.1	6	0
DU M															
SD		31.6	19.9	18.4	1.6	22.3	24.2	1.4	21.4	22.6					
=		1000	398	347		496	557		466	503				1.0	
B															
D.U M	7	29	124	120	6	37	52	4	87	87	13	89	1.5	6	0
SD		15.2	8.2	8.9	1.8	8.9	15.0	1.0	15	14.2				1.6	
=		233	68	79		79	227		224	200					
VC M															
	6	38	97	85	7	30	46	6	67	43	50	33		7	33 $\frac{1}{3}$
SD		15.6	24.3	24.0	1.0	17.6	23.0	.2	22.0	18.0				1.0	
=		247	586	533		305	521		483	323					
AV M	11	33	107	103	7	37	59	4	70	57	24	26		7	0
SD		14.3	25.9	25.2	1.0	22.0	24.3	1.6	15.3	20.4				1.3	
=		215	660	639		481	557		233	424					
P.A. M	3	40	73	51	5	20	19	3	53	31	4	15	0	7	100
S.D.		16.2	.26	13.8	2.5	6.2	2.0	0	9.0	18.0				1.0	
=		267	0.67	188		422	4		81	325					
F. M	16	25	98	101	7	27	47	5	71	67	28	19	0	7	25
S.D.		11.2	18.3	19.2	1.2	10.0	16.7	1.3	18.3	22.0				1.0	
=		130	331	368		101	273		339	480					

SD = Standard Deviation
B = Postoperative.

M = Mean
A = Preoperative

RESULTS OF INVESTIGATIONS.

Average findings in 10 normal cases -

Fasting juice : - volume 32 c.c.

Curve of concentration of total chlorides - fasting level 91, (c.c. of N/10 NaOH per 100 c.c. of contents) rising after ingestion of the meal to approximately the same level in one and a half hours, and maintaining this during the remainder of the investigation.

Curve of total acidity:- fasting level 33, rising, parallel with curve of total chlorides, to nearly twice this height, in one and a quarter hours, and tending thereafter to fall more or less abruptly.

Curve of concentration of neutral chloride - Fasting level relatively constant, 59; remaining low during increase of acidity, later rising to a terminal level somewhat lower than that noted in the fasting-juice.

Mucus in 20% of specimens; bile in 26%.

Blood absent throughout.

Emptying-time (as indicated by disappearance of starch) - one and three quarter hours.

In three cases there were significant departures from the mean of the group: -

N/

N/₂₂ - The emptying-time was reduced.

N/₄₄ - The fasting level of total chlorides and the highest attained acidity were both low.

N/₈ - Bile was present in every specimen.

GASTRIC ULCER GROUP.

(a) Before operation; -

Highest attained total chloride level and terminal neutral chloride level were relatively constant. There was no significant difference from the normal.

(b) After Operation:- (gastroenterostomy)

The terminal neutral chloride level was relatively constant.

Significant differences from the preoperative figures were the lowering of the highest acidity attained, the increase of the terminal neutral chloride level and the more frequent appearance of bile.

CARCINOMA OF STOMACH GROUP.

The fasting level of total chloride, the fasting level and highest attained total acidity and the fasting level of neutral chloride were relatively constant. Achlorhydria was constant.

Significant differences from the normal were the low acidity attained after ingestion of the meal/

meal, the high percentage of mucus, the frequent occurrence of blood and the presence of achlorhydria in all cases examined.

CHRONIC PRIMARY GASTRITIS GROUP.

Relatively constant findings were: - fasting juice volume, initial and highest attained levels of total acidity, and terminal neutral chloride. Achlorhydria was constant.

Significant differences from the normal were: - the low figures for initial and highest attained levels of total chlorides and total acidity, highest attained level of neutral chloride, the frequency of the appearance of mucus and, in every case, the occurrence of achlorhydria.

One case, after medical treatment, showed significant decrease in mucus, otherwise no alteration was noted.

CHRONIC DUODENAL ULCER GROUP.

(a) Preoperative -

No constant features were noted.

Significant differences from the normal were the increased fasting level of hydrochloric acid, and the presence in a small number of specimens, of blood. In one case a fasting-juice content of/

of 850 c.c. was found.

(b) Postoperative -

Constant features were the fasting and highest attained levels of total chlorides and the fasting level of total acidity.

Suggestive, though not significant, differences after gastroenterostomy were the decreased fasting-juice volume, the increased fasting and terminal levels of neutral chloride, and the increased frequency in appearance of bile.

CHOLELITHIASIS GROUP.

No constant features were noted.

Significant differences from the normal were the decreased level of total acidity and the occurrence of achlorhydria in one third of the cases.

CHRONIC APPENDICITIS GROUP.

No constant features were noted.

There was no significant difference from the normal.

PERNICIOUS ANAEMIA GROUP.

Constant features were the fasting levels of total chloride and total acidity, the highest attained level of total acidity, the initial level of neutral/

neutral chloride and the occurrence of achlorhydria.

Significant differences from the normal were: -

Decrease of the highest attained levels of total chlorides and total acidity, and the occurrence in all cases of achlorhydria.

FUNCTIONAL GROUP.

The fasting level of total acidity was relatively constant. Apart from the occurrence of achlorhydria in one quarter of the cases, there was no significant difference from the normal.

MISCELLANEOUS GROUP.

Significant differences from the normal: -

- M 1. (Jejunal Ulcer): an increased fasting-juice volume and a raised fasting level of neutral chloride.
- M 2. (Multiple Tuberculous Strictures of Small Intestine): decreased emptying-time.
- M 3. (Carcinoma of Head of Pancreas): decreased level attained by total acidity, decreased fasting level of neutral chloride, and presence of achlorhydria.
- M 4. (Carcinoma of Head of Pancreas): no significant difference.
- M 5. (Chronic Pancreatitis): no significant difference.
- M 6. (Catarrhal Jaundice): raised fasting levels of total chlorides and of neutral chloride.

M/

- M/7. (Spirochaetal Cirrhosis of Liver): - raised fasting level of neutral chloride.
- M/8. (Spirochaetal Cirrhosis of Liver): - raised fasting and terminal levels of neutral chloride.
- M/9. (Malignant Peritonitis): - raised fasting levels of total chlorides and total acidity.
- M/10. (Malignant Peritonitis): - raised fasting levels of total and neutral chlorides and raised terminal level of latter.
- M/11. (Carcinoma of Caecum):- no significant difference.
- M/12. (Carcinoma of Pelvic Colon): - decreased fasting level of neutral chloride.
- M/13. (Renal Calculus): - no significant difference.
- M/14. (Petit Mal): - raised terminal level of neutral chloride. Presence of Achlorhydria.
- M/15. (Chronic Iritis): - no significant difference.
-

DISCUSSION/

DISCUSSION OF RESULTS.

An attempt will be made to define the utility of these investigations in differential diagnosis and in the study of the effects of operation. Thereafter, the mechanism of control of gastric acidity will be discussed in the light of the results obtained.

The wide variation shown in the form of the curves of the normal series is an indication of the necessity for examination, by a standard method, of a large series of cases.

So far as can be ascertained, the literature contains no detailed results of investigation, suitable for comparison with the present series. It is true that certain conclusions have been published by BOLTON & GOODHART^(9, 10), BAIRD, CAMPBELL & HERN⁽²⁾, MILLER & SMITH⁽⁴⁹⁾, STEINITZ⁽⁷³⁾, and ROTHSCHILD⁽⁶⁶⁾, and, but, in general, these authors quote no actual figures, and employ various 'meals'; in one case⁽⁴⁹⁾, a system of classification, based on the form of the curve of 'free' hydrochloric acid, is adopted.

DIFFERENTIAL DIAGNOSIS.

(1) Of Gastric and Duodenal Ulcer -

A high fasting level of total acidity is suggestive/

suggestive, though not conclusive of duodenal ulcer.

(2) Of Gastric Ulcer and Carcinoma.

The formula of GRAHAM⁽²⁵⁾, that the ratio of acid to neutral chloride is greater than unity in ulcer, and less than unity in carcinoma of the stomach, here holds good only at the height of the acid curve, not in the fasting juice. Ratios less than unity are obtained in pernicious anaemia and gastritis in addition to carcinoma, so that a differentiation of these three conditions, by this formula, is not possible.

(3) Of Carcinoma of the Stomach, Pernicious Anaemia and Gastritis, - relatively high values for total chlorides and total acidity, together with the occurrence of blood, are strongly indicative of carcinoma.

No clear distinction can be drawn by the estimation of the chlorides, between gastritis and pernicious anaemia; great increase of mucus, however, is favourable to diagnosis of the former condition.

(4) Of the foregoing group and other cases of Achlorhydria.

The detection of blood and increase of mucus or, of increase of mucus alone, suggests carcinoma or gastritis, respectively. The Achlorhydria of Pernicious Anaemia cannot be distinguished from the achlorhydria of conditions other than carcinoma or gastritis.

RESULTS OF GASTROENTEROSTOMY FOR ULCER.

Bile occurs more frequently in duodenal ulcer, and here there is an increased concentration of neutral chloride throughout. Reduction of acidity, however, is proportionately greater in gastric ulcer.

COMMENT.

Further knowledge is required before a just evaluation of this method in differentiating the achlorhydric group is possible.

Light may be thrown upon the occurrence of jejunal ulcer after gastroenterostomy, by employing this means of investigation in a large series of cases of gastric and duodenal ulcer undergoing the operation; special interest would attach to those in which jejunal ulcer developed.

THE CONTROL OF GASTRIC ACIDITY.

The acidity of the pure gastric juice in man has been estimated by SCHEUNERT, quoted by REHFUSS (58, p.56), at 0.5% HCl. (41). LIM, however, concludes from an investigation of the normal human gastric response to histamin, that the acidity of the juice is 0.35% HCl. The acidity of normal gastric contents is generally agreed to be 0.1 to 0.2% of 'free' hydrochloric acid.

Shortly after the ingestion of a meal and the commencement of active secretion, the acidity of the contents is low as the first portions of juice secreted are diluted by the meal. The acidity tends to rise as secretion continues and the stomach empties because there is progressive replacement of food by a highly-acid secretion. ?

The greatest mean total acid values of the gastric contents in the writer's normal series were only 0.19% 'free' hydrochloric acid, and this usually preceded a fall. Some regulating mechanism must therefore exist to prevent the attainment, by the gastric contents, of an acidity equal to that of the pure juice.

The three principal theories relating to this/

this mechanism have already been outlined; it is proposed to examine them, firstly as regards criticisms by the opponents of each, and secondly in relation to phenomena noted in the course of the investigations.

BOLDIREV believes that the pure gastric juice has a constant acidity, as stated by PAVLOV, and that the acidity of the gastric contents is prevented from exceeding the optimum by the regurgitation of alkaline duodenal contents. The first doubts were cast on this explanation by HICKS & VISHNER⁽³³⁾, who studied the mechanism of regurgitation in cats; they sometimes noted a fall in concentration of acid introduced into the stomach, although bile did not appear.

MORRELL ROBERTS⁽⁶⁰⁾, found that atropine in his patients frequently lowered the acidity and ~~of the~~ gastric contents and raised the concentration of neutral chloride in the absence of bile. Recently, DUTHIE⁽¹⁸⁾ has stated that in his fractional analyses reduction of acidity and increase in neutral chloride values occasionally occurred without the appearance of bile.

From a study of the hundred charts representing investigations in the present series it was found that: -

(1)/

- (1) Reduction of acidity (by 10 or more c.c. N/10 NaOH) took place in the complete absence of bile after the ingestion of the meal in 22% of all investigations;
- (2) the appearance of bile coincided with reduction of acidity in 14%;
- (3) bile was present immediately preceding and following reduction in 12%;
- (4) bile appeared independently of reduction in 60% of investigations. As an example: - bile might appear early in the test and again later, possibly coinciding with reduction.

From this, reduction of acidity and appearance of bile do not appear to be closely related.

A satisfactory explanation would be given of this lack of close correspondence if it were supposed that pancreatic alkali might regurgitate into the stomach unaccompanied by bile.

Evidence relating to this possibility is scanty and inconclusive. ^(7, p.5) BOLDIREV stated that reduction in the concentration of acid introduced into the stomach of dogs often took place when the contents "were but little coloured by bile".

⁽⁷²⁾ REHFUSS, investigating the presence of trypsin in stomach-contents noted that a rise in tryptic values could occur in the absence of bile which might "variously be interpreted as due possibly to a difference in the elimination of bile and pancreatic secretion, or to the specific reflux of/

of the pancreatic secretion alone".

It is difficult, however, to admit the existence in the duodenum of pancreatic secretion unmixed with bile. Secretion of bile is a continuous process and the requisite relaxation of the sphincter of Oddi to permit the outflow of pancreatic secretion would involve also the liberation of bile.

That a dissociated regurgitation of this nature can occur is denied by MacLEAN⁽⁴³⁾.

Interaction of hydrochloric acid and sodium carbonate - the alkali of the pancreatic secretion - is, he states, accompanied by a demonstrable increase in the gastric contents of dissolved carbon dioxide. In a series of investigations, he found that bile always appeared simultaneously with such an increase, and that, in the absence of bile, no increase could be detected.

MacLEAN concludes from this that no pancreatic alkali is regurgitated into the stomach unaccompanied by bile.

This evidence supports the view that a dissociated regurgitation of bile and pancreatic secretion does not occur. Further investigation, however, is required before a dogmatic statement can be made.

The second theory will now be examined regarding the explanation of the form of the various curves.

To recapitulate, the fall in acidity of the gastric contents is therein held to be brought about by dilution with a juice of diminishing acidity; the supporters of this theory further hold that the total chlorides concentration of the juice is constant, therefore neutral chloride must be secreted along with acid and in inverse proportion to it. Fall in acidity, therefore, according to this view, is accompanied by increased secretion of neutral chloride.

If the existence of a sufficiently wide variation in acidity of the secreted juice can be demonstrated, a completely satisfactory explanation of the mechanism of control of gastric acidity is provided.

(8)
BOLTON, however, denies that this is so. (43)
He criticises MacLEAN'S conclusions, drawn from observations upon the secretion of isolated gastric pouches, on the grounds that the lowest figure recorded for acidity of the juice, while lower than those of previous observers, remained higher than the highest level attained by the gastric contents; and that therefore the juice could not, by dilution, diminish/

diminish the acidity of the contents. He reiterated the view of PAVLOV that variations in acidity of the secretion from a 'pouch' were entirely due to the neutralising effect of the alkaline gastric mucus. In the same way, he stated, ROSEMAN⁽⁶²⁾'S results did not, at any time, demonstrate an acidity of the juice sufficiently low to decrease the acidity of the gastric contents.

In support of the contention that the acidity of the juice remains constant, he quoted results obtained from a case of 'hour-glass' stomach in which the constriction was situated about the middle of the viscus. The upper and lower sacs were simultaneously intubated, the positions of the tubes being confirmed by radiosopic examination. The curve of acidity in the proximal sac rose steadily; that in the distal sac remained low, the concentration of sodium chloride being consistently high. Bile appeared only in the contents of the lower sac, and BOLTON held that this was clear evidence that duodenal regurgitation was necessary to reduce the acidity of gastric contents.

It appeared to the writer that another interpretation could be placed on these findings. HEILMEYER⁽³²⁾ believes that two separate cells exist for the production of hydrochloric acid and neutral chloride, respectively. If it could be shown that these/

these theoretical cells for the secretion of neutral chloride were distributed in the lower half of the stomach, a satisfactory explanation could be given of the markedly increased neutral chloride concentration in the lower sac of BOLTON'S case, as compared with the upper.

So far as could be ascertained, there existed in the literature no reference to a gastric pouch, with nervous connections intact, situated in the lower half of the fundus of the stomach, as distinct from the pouch of PAVLOV constructed in the upper half. It is true that the fundus-pouch of HEIDENHAIN occupied the lower position but the operation involved division of the nerves in the wall of the stomach. A method was therefore selected which enabled an isolated pouch to be formed without division of the muscular layer of the posterior wall and the nerves running therein.

At the commencement of animal-experimentation the writer was unaware of the work of GAMBLE (23, 24) and McIVER upon the composition of the secretion obtained from an isolated pouch of the entire pyloric segment; these observers noted a concentration of neutral chloride in the secretion approximating that of the blood-plasma.

This finding will again be referred to
(p. 56).

The/

The original intention of the experimental work was to construct two gastric pouches in the same animal, for the purpose of obtaining samples of pure secretion from the upper and lower halves of the stomach simultaneously. In this way any difference in the acidity of the respective secretions could be detected.

The low fundus-pouch was first constructed and, after recovery of the animal, investigations were carried out upon the secretion obtained. Later a 'PAVLOV-pouch' was formed in the same stomach, but the animal died from post-operative pneumonia.

The technical possibility of constructing two such pouches in the one stomach was, however, demonstrated.

In selecting experimental material, attention was paid to two points, firstly, that the physical type of the animal should permit of easy surgical access - a relatively short dorso-ventral diameter of the thorax being found preferable - and secondly, that 'free' hydrochloric acid should be present in the gastric contents.

The details of operation and experimental investigations, together with charts, diagrams and photographs will be found in an appendix. By the introduction of micro-methods it was possible to obtain/

obtain reliable figures for total chlorides, total acidity, neutral chloride and pepsin quarter-hourly. Had it been required, the interval could have been shortened; 0.6 c.c. was the actual quantity necessary for the estimations.

RESULTS OF EXPERIMENTS.

Curves of concentration for various components of the secretion were obtained with different foodstuffs. The pepsin-variations are considered separately (p. 59).

DESCRIPTION OF CURVES.

Volume: - this curve showed an initial rise and a gradual fall; the quantities were approximately directly proportional to the amount of food of any one kind administered. Thus, for 75 G. of dog-biscuit the mean volume of the quarter-hourly specimens was 1.66 c.c.; for 45 G. biscuit the mean volume was 0.66 c.c. Bringing these figures in each case to the volume calculated for 100 G. biscuit the figures for the larger meal were 2.21 c.c. and for the smaller 2.88 c.c. per specimen.

Concentration of total chlorides: - The average value of all the samples was 150 (c.c. N/10 NaOH, per 100 c.c. juice) being highest with a/

a meat-meal and lowest with a small biscuit-meal. The curve rose somewhat at the beginning of active secretion and fell, but to a less extent, at the end of two hours.

TOTAL ACIDITY.

The average concentration was 122. There was usually a sharp initial rise, followed by a gradual and smaller fall. A sharp fall occurred with a small biscuit meal, the terminal figure, 79, being the lowest recorded in the series.

NEUTRAL CHLORIDE CONCENTRATION.

A decrease at the beginning of the test, was followed by a moderate increase which exceeded the initial level only in the case of the small-biscuit-meal.

Quantitative figures for the various components were obtained, in terms of c.c. of N/10 NaOH by multiplying the concentrations of each by the volumes of the samples.

This was done in the case of three meals of which the figures are given below. For comparison, the concentration - figures are placed in brackets next to each quantitative value.

TABLE/

200 G. BISCUIT, MEAT and MILK IN EQUAL PARTS.

	<u>Total Cl</u>	<u>Total HCl</u>	<u>NaCl</u>
$\frac{1}{4}$ hr.	47.36 (147)	32.64 (102)	14.72 (45)
$\frac{1}{2}$ hr.	69.30 (153)	54.00 (120)	15.30 (33)
$\frac{3}{4}$ hr.	60.04 (159)	46.36 (122)	13.68 (37)
1hr.	58.09 (158)	45.61 (124)	12.48 (34)
$1\frac{1}{4}$ hr.	38.00 (152)	32.50 (130)	5.50 (22)
$1\frac{1}{2}$ hr.	30.40 (153)	25.40 (127)	5.00 (26)
$1\frac{3}{4}$ hr.	22.80 (153)	18.60 (124)	4.20 (29)
2hrs.	<u>23.68 (148)</u>	<u>17.92 (113)</u>	<u>5.76 (35)</u>
Mean	<u>23.94 (153)</u>	<u>19.43 (120)</u>	<u>4.51 (33)</u>

75 G. BISCUIT

$\frac{1}{4}$ hr.	26.40 (133)	14.60 (73)	11.80 (60)
$\frac{1}{2}$ hr.	34.75 (139)	29.50 (118)	5.25 (21)
$\frac{3}{4}$ hr.	29.60 (148)	26.60 (133)	3.00 (15)
1hr.	34.96 (152)	31.28 (135)	3.68 (17)
$1\frac{1}{4}$ hr.	26.46 (147)	21.96 (122)	4.50 (25)
$1\frac{1}{2}$ hr.	15.20 (152)	12.80 (128)	2.40 (24)
$1\frac{3}{4}$ hr.	25.56 (142)	21.42 (119)	4.14 (23)
2hrs.	10.50 (150)	7.84 (113)	2.66 (37)
$2\frac{1}{4}$ hrs.	<u>12.00 (150)</u>	<u>8.88 (111)</u>	<u>3.12 (39)</u>
Mean	<u>43.71 (146)</u>	<u>34.13 (117)</u>	<u>9.58 (29)</u>

45 G. BISCUIT.

$\frac{1}{4}$ hr.	28.40 (141)	16.60 (83)	11.80 (58)
$\frac{1}{2}$ hr.	9.36 (156)	4.98 (106)	4.38 (50)
$\frac{3}{4}$ hr.	10.15 (144)	7.56 (107)	2.59 (37)
1hr.	8.52 (144)	7.80 (130)	0.72 (14)
$1\frac{1}{4}$ hr.	10.92 (156)	6.72 (96)	4.20 (60)
$1\frac{1}{2}$ hr.	14.80 (148)	8.50 (85)	6.30 (63)
$1\frac{3}{4}$ hr.	-	-	-
2hr.	13.32 (148)	7.11 (78)	6.21 (70)
Mean	<u>13.64 (148)</u>	<u>8.47 (98)</u>	<u>5.17 (50)</u>

An/

An interesting fact was observed in examining these quantitative figures, namely that the amount of total chloride secreted is directly proportional to the quantity of food of a particular kind given. If the mean figure for total chlorides be multiplied by $100/75$ in the case of the meal of 75 G. of biscuit, and by $100/45$ in the meal of 45 G. of biscuit, the figures 31.92 and 30.31 respectively are obtained.

This close correspondence disappears when the figures for the other two constituents are similarly treated, 25.91 and 18.82, for acid, 6.01 and 11.49 for neutral chloride, being obtained. The ratio of acid to neutral salt is much less in the case of the smaller meal.

No reference to values of chlorides and acid expressed in quantities, has been met with in the literature.

There is no evidence from the investigations, of a predominance in the lower half of the fundus of cells secreting neutral chloride. The findings of GAMBLE and McIVER, ^(23,24) previously alluded to, acquire, therefore, an added significance (see p. 56.)

The/

The lowest terminal figure for acidity, 79, was obtained in the small biscuit-meal. With a slightly smaller meal (40 G. biscuit) MacLEAN observed a terminal acidity of 68.

In a fractional gruel test-meal administered to the animal 25 days before operation the highest acidity noted in the gastric contents was 60.

BOLTON'S criticism, therefore, that the acidity of the juice does not fall low enough to decrease that of the contents, seems justified.

The curves of acid-concentration obtained by the writer differ from those published by MacLEAN in two particulars. The first of these is the marked initial increase in acidity noted in this series; the second is the absence, except in the case of the small biscuit meal, of the sharp interterminal decline described by MacLEAN.

In contrast, also, with the uniform figures given by MacLEAN for total chlorides, the writer found an initial rise similar to that of the acidity, though less marked, and a slight fall towards the end of the experiment.

There are two possible explanations for this rise and fall. Firstly, the concentration of total chlorides in the freshly-secreted juice may be relatively low at the beginning and at the end of secretion./

secretion. Secondly, dilution of the juice, in which the concentration of total chlorides is assumed to be constant, may have taken place subsequently to secretion, the process affecting chiefly the early and late samples. A possible diluent is known to exist in the form of gastric mucus.

According to this latter view, the first portions of the secretion mix with, and are diluted by, mucus. As this mucus tends to be removed by the continuous washing action of secretion the later samples of juice are less exposed to such dilution than the earlier.

If the initial low figures for total chloride concentration indicate dilution, the figures for acidity will be similarly affected. In addition to its diluent effect, mucus, by reason of a slight alkaline reaction will tend still further to reduce acidity by neutralisation.

The alkalinity of gastric mucus is given by GAMBLE and McIVER^(23,24) as approximately 5c.c. N/10 NaOH per 100 c.c.

In the case of the meal of 75G. biscuit the initial total chlorides concentration was 133 per 100 c.c. of juice; in one hour this rose to 152. If the smaller figure was due to dilution, by mucus, of/



of a juice of concentration 152 per 100 c.c. this volume must have been increased to $100 \times \frac{152}{133} = 115$.

N.B. Mucus dilutes total chlorides of secretion rather less than distilled water (BOLTON) Therefore the diluting volume of mucus is slightly greater than 15 c.c.

Then 100 c.c. of juice were diluted by 15 c.c. mucus. The acid concentration at the end of one hour was 135. If 100 c.c. of a juice of acidity 135 are diluted by 15 c.c., of mucus the resulting concentration is $135 \times \frac{100}{115} = 117$. But, since 100 c.c. of mucus have a neutralising power of 5 c.c. N/10 NaOH the acidity is still further reduced by neutralisation to the extent of $5 \times \frac{15}{100} = 0.75$ c.c. N/10 NaOH = 0.75 c.c.

Therefore, by combined dilution and neutralisation a juice of 135 acid-concentration is reduced to 116.25.

This is still considerably above the observed figure, which is 73.

It may be held that no allowance has been made for acid in combination with the protein of mucus. This is not a valid objection as the total acidity is estimated by titration with phenolphthalein and includes hydrochloric acid both 'free' and adsorbed on to protein.

The/

The evidence, therefore, seems to indicate that variations of acidity in the freshly-secreted juice do occur, and that mucus, largely by its diluent action may cause further variations.

They do not appear sufficient, however, to bring about reduction in acidity of gastric contents.

The third view, that the secretion of the pylorus provides an alkali which neutralises excess of acid, will now be examined.

Experimental work on the pyloric segment has always been hampered by the difficulty of devising a pouch similar in principle to that constructed by PAVLOV, in the fundus. Owing to the restrictions imposed by size, it has been necessary to form a pouch consisting of the whole pyloric segment; continuity of the alimentary canal is restored by gastroenterostomy.

As obtained from such an isolated pouch, the pyloric secretion is scanty, 1-5 c.c. per hour
 (35) (30)
 (IVY; HEIDENHAIN, (35), glairy and slightly alkaline, (30)
 the pH being 7.5 (IVY HEIDENHAIN 30). The alkali is sodium carbonate.

The application for 5 minutes of 0.5% HCl or of pure gastric juice increases the secretion approximately/

approximately three times. This suggests that the pyloric segment, in continuity, is considerably more active than when isolated.

(2)

BAIRD, CAMPBELL and HERN published results of a case "M.B" in whom regurgitation of duodenal contents was prevented by intubation of the duodenum; in spite of this the acidity of the gastric contents fell. They ascribed this result to the neutralising action of the alkaline pyloric secretion.

(55)

POULTON (55) believes that there is insufficient alkali in the pyloric secretion for adequate neutralisation of the gastric hydrochloric acid.

His criticism of the conclusions of BAIRD and his colleagues is as follows:

"Taking the true or active HCl as the average of the total and free acids (as recommended by them in Appendix 2) we find that 100 c.c. of gastric contents were equivalent to 17 c.c. N/10 NaOH, and contained 0.06 G. Cl. Similarly, there was 0.29 G Cl as total chloride, and the mineral chloride was the difference - namely, 0.23 G. Cl; 0.343G. $\text{Na}_2 \text{CO}_3$ would have been required to produce this mineral chloride from the gastric HCl.

"We will assume that pure gastric juice (containing/

containing 0.5% HCl or 0.486 G per cent Cl) was being secreted by the stomach at this point, and that this and the alkali required to neutralise it were the only fluids present, while the fluid of the meal had been passed into the duodenum. Then the alkali must have diluted the gastric juice in the ratio of 29 to 48.6 - that is, 59.6 c.c. were diluted up to 100 c.c., which means that the neutralising alkali containing 0.434 G. $\text{Na}_2 \text{CO}_3$ was contained in 40.4 c.c. of fluid, so that the stomach secreted a juice containing 0.85% $\text{Na}_2 \text{CO}_3$ ".

This being well above the highest alkalinity recorded for even the pancreatic secretion, POULTON concluded that neutralisation could not account for the whole of the mineral chloride found, and that a more reasonable explanation was the secretion of this substance by the stomach itself.

(43)

MacLEAN, found that reduction of gastric acidity could occur without any evidence, in the form of increased carbon dioxide in solution in the gastric contents, of neutralisation of hydrochloric acid by sodium carbonate. He concluded that neutralisation of acid by alkali is not essential for reduction.

It was observed also that increased formation of carbon dioxide could not be detected in the absence/

of bile. It would thus seem probable that neutralising alkali is derived almost entirely from the mixed secretions in the duodenum, and that the alkali of the pyloric segment plays a relatively unimportant part.

An alternative to the theory of neutralisation by pyloric alkali is here put forward, namely, that the pyloric segment itself secretes sufficient neutral chloride to effect an appreciable reduction in the acidity of the gastric contents by dilution.

The high concentration of neutral chloride in the pyloric secretion has been shown by GAMBLE and McIVER,^(23.24) and the previously-quoted experiment of IVY and OYAMA⁽³⁵⁾ suggests that the pyloric segment, in continuity, may produce enough secretion of a diluent nature to cause partial reduction of gastric acidity. The slight alkalinity of the secretion would still further diminish acidity by neutralisation.

A review of the three theories relating to the mechanism of gastric acidity-control leads the writer to believe that none, by itself, is likely to provide an adequate explanation.

In the clinical investigation, regurgitation of alkaline duodenal contents did not appear essential to reduction of gastric acidity; on the other hand/

otherhand, there was no indication from the results of animal-experiments that there is a sufficient diminution in the acidity of the secreted juice to reduce, by dilution, that of the gastric contents. Finally, it is probable that the pyloric juice does not contain sufficient alkali appreciably to reduce the acidity of the gastric contents, and further that this secretion is a diluting rather than a neutralising agent.

The writer is of the opinion that the mechanism of gastric acidity-control is to be regarded as depending upon several contributory factors. The explanations at present advanced separately are believed to be compatible one with another. Probably there are additional factors to be taken into account.

The following are regarded as influencing the concentration of acid in the gastric contents:

- (a) ingested material (food and saliva), and gastric mucus the effect of these is mainly diluting, although neutralisation may occur to a slight extent;
- (b) variation in acidity of the fundus-secretion - the juice secreted during the first "phase" of gastric/

gastric digestion rapidly acquires a high degree of acidity in order to accelerate the production of the "optimum" level of acidity in the gastric contents; when this object is achieved the acidity of the secretion diminishes;

- (c) the pyloric secretion - the effect of this is believed to be reduction of gastric acidity by a process of dilution, neutralisation playing a minor rôle;
- (d) alkaline duodenal regurgitation - this reduces acidity by combined neutralisation and dilution;
- (e) gastric motility - a quickly-emptying stomach by speedy removal of the diluent action of ingested material, causes the acidity of the gastric contents more rapidly to approach that of the pure secretion. Conversely, a slowly-emptying stomach prolongs the intermixture of ingesta and secretion, thus retarding the development of the optimum level of acid-concentration in the stomach.

The mechanism controlling gastric acidity in health depends, in all probability, upon the harmonious co-ordination of some or all of these contributory factors.

PEPSIN-VARIATIONS.

The investigations of the proteolytic action of the gastric secretion, though admittedly of consequence, is not, as a rule, performed in the examination of cases.

This is largely because existing methods for estimating peptic activity are often unduly time-consuming; further they may require elaborate and expensive apparatus.

The introduction of a simple method, therefore, should be of considerable value in extending the scope of gastric analysis.

Estimations of pepsin, in both experimental and clinical material, have been performed with the object of gaining insight into the significance of pepsin-variations in health and disease.

Many of the workers who laid the foundations of our knowledge of the acid in the gastric secretion, at the same time established certain facts relating to the digestive power of the juice.

REAUMUR⁽⁵⁷⁾, in 1752, demonstrated partial disintegration of grain, contained in *perforated metal capsules, and placed in the stomach of birds which/

which were killed after a short interval of time.
 SPALLANZI⁽⁷¹⁾, obtaining specimens of stomach contents from various animals, found that a similar effect could be observed in vitro. BEAUMONT (quoted by OSIER⁽⁵¹⁾), found the human juice "an effective solvent of the materia alimentaria".

The credit for the first full investigation of this property of the gastric secretion is due to SCHWANN⁽⁶⁹⁾, who, in 1836, clearly demonstrated certain conditions essential to the process. SCHWANN believed that the juice contained an active 'principle'; WASMAN⁽⁷⁵⁾, attempted unsuccessfully to isolate this. BRUCKE⁽¹²⁾, was the first in 1862, to obtain a relatively pure preparation of Pepsin, as the 'principle' was named.

HEIDENHAIN⁽³¹⁾, in 1879, enunciated the view that certain large cells of the gastric mucosa, the 'chief' or 'central' cells, are responsible for the production of pepsin.

KLEMENSIEWICZ⁽³⁸⁾, HEIDENHAIN⁽³⁰⁾, and ACKERMANN⁽¹⁾, reported the finding of a proteolytic secretion from the isolated pyloric segment, although this was generally agreed to be less active than the secretion from fundus-tissue proper.

In 1879, LANGLEY & SEWALL⁽³⁹⁾, demonstrated/

demonstrated the presence of 'zymogen' granules, believed to be fore-runners of the enzyme, in the cytoplasm of the 'central' cells of the fundus mucous membrane and described their diminution during digestion. These workers were unable to find granules in the corresponding cells of the pyloric mucous membrane. There has been considerable discussion regarding the proteolytic nature of the pyloric juice. BENSLEY quoted by IVY & OYAMA⁽³⁵⁾, holds that it has no peptic activity, while LIM & DOTT⁽⁴⁰⁾, affirm the original view of KLEMENSIEWICZ & HEIDENHAIN.

METHODS for PEPSIN ESTIMATION.

These have been placed in two main groups modified from the classification of WAKSMAN & DAVISON⁽⁷⁴⁾.

- (a) The determination of the amount of protein digested at the end of a given time, and -
- (b) The determination of the quantity of test-solution which contains a particular amount of enzyme, i.e. the amount which causes hydrolysis of a definite amount of protein in a given time.

This classification is now applied to the methods under consideration.

- (a) The amount of protein digested in a given time may be estimated in the following ways:-

1. By the measurement of an amount of insoluble solid/protein

solid protein which remains unliquefied; in the method of ⁽⁴⁸⁾METTE, this can be calculated by observing the height of the digested column of coagulated egg-white in capillary-tubes.

2. By the titration of a solution or suspension of protein in order to determine the amount which remains undigested: ⁽²⁷⁾HAMMERSCHLAG, estimates the undigested protein in 1% egg-albumin solution measuring the amount precipitated by adding Esbach's solution;

3. By the measurement of the products of digestion.
⁽⁶⁸⁾

- i. J. SCHUTZ ⁽⁶⁸⁾, precipitated unchanged albumin and acid albumin, then estimated, by Kjeldahl's method, the nitrogen remaining in solution;
- ii. E. SCHUTZ ⁽⁶⁷⁾, after similar precipitation, observed the amount of laevo-rotation due to protein in solution;
- iii. GRÜTZNER ⁽²⁶⁾, and CITRON ⁽¹⁵⁾, estimated colorimetrically the amount of a dye-stuff liberated during digestion of protein. The former used fibrin saturated with carmin, the latter fibrin saturated with 'fibrochrome' a blue dye;
- iv. ROSTOCK ⁽⁶⁴⁾, measured the increase in refractive index of the solution after digestion;

v. BOAS⁽⁵⁾, measured the volume of starch set free by the peptic digestion of macaroni;

4. By following the course of digestion at intervals, having regard to physical changes in the protein solution: RONA & KLEINMANN⁽⁶¹⁾, estimated at definite intervals by means of the nephelometer the degree of turbidity existing in the protein solution.

b. The smallest quantity of test solution required to hydrolyse a definite amount of protein may be determined by the following methods: -

- i. FULD & LEVISON⁽²²⁾, determined the smallest amount of enzyme required to digest in thirty minutes, 2 c.c. of an 0.1% solution of edestin (the protein of hemp seed);
- ii. HATA⁽²⁹⁾, found the smallest amount of enzyme required to discharge the opalescence of a measured volume of egg-white suspension.
- iii. In this group also is included the method recently introduced by W.O.KERMACK.

This depends upon the removal of protein by digestion, from a mixture containing fixed amounts of colloidal gold solution, protein and hydrochloric acid. Precipitation of gold by the acid is prevented if sufficient protein be present, and therefore follows removal of this protective action. The reddish/

reddish-pink colour of the mixture undergoes alteration or is completely discharged, according to the degree of precipitation; this, in turn, depends upon the amount of protein removed by digestion. Hydrochloric acid serves two purposes; it precipitates unprotected colloidal gold, and provides a hydrogen-ion concentration suitable for peptic digestion.

TECHNIQUE.

Twelve small clean test-tubes are set up in a rack and numbered. Into each in the following order is placed, 0.5 c.c. of colloidal gold solution (as used in the LANGE test on cerebro-spinal fluid) 0.2 c.c. of ox serum, and 0.5 c.c. N/5HCl. To tubes 1, 2, and 3, are added 0.5, 0.2 and 0.1 c.c. respectively of filtered gastric contents, or test solution. To tubes 4, 5, and 6, are added 0.5, 0.2 and 0.1 c.c. respectively of the contents diluted 1 in 10 with distilled water.

Corresponding quantities of dilutions 1 in 100, and 1 in 1000, in distilled water are added to tubes 7, 8, and 9, and 10, 11 and 12 respectively.

To the second and third tubes in each group of three are added 0.3 and 0.4 c.c. respectively of distilled/

distilled water, so as to equalise the volumes of the whole series.

The tubes are agitated in order to mix the components.

The rack is then placed in the incubator and kept at a constant temperature of 37°C for twenty-two hours.

Readings are taken at the end of this time, and the last tube in which complete precipitation has occurred, as shown by the discharge of the pink colour, is noted.

For example, if complete precipitation last occurred in tube 6 (containing .01 c.c. of test solution) the concentration of the enzyme would be 100 times that of one requiring 1 c.c. to effect the same change. This result may be expressed as 100 'units'. Similarly, if precipitation last occurred in tube 10 (containing .0005 c.c. test solution) this represents a concentration in the enzyme of 2000 'units'.

By determining the activity of a commercial standard preparation, it is possible to express results in terms of c.c. of this standard.

Thus a 10% glycerin extract of pepsin (Armour) was found, by this method, to have an enzyme-concentration of 1000 'units'. 100 c.c. of gastric contents/

contents of equal activity are then equivalent to 100 c.c. of the standard; 100 c.c. of a gastric contents of 50 'units' activity are, in the same way equivalent to 5 c.c. of the standard.

DISCUSSION/

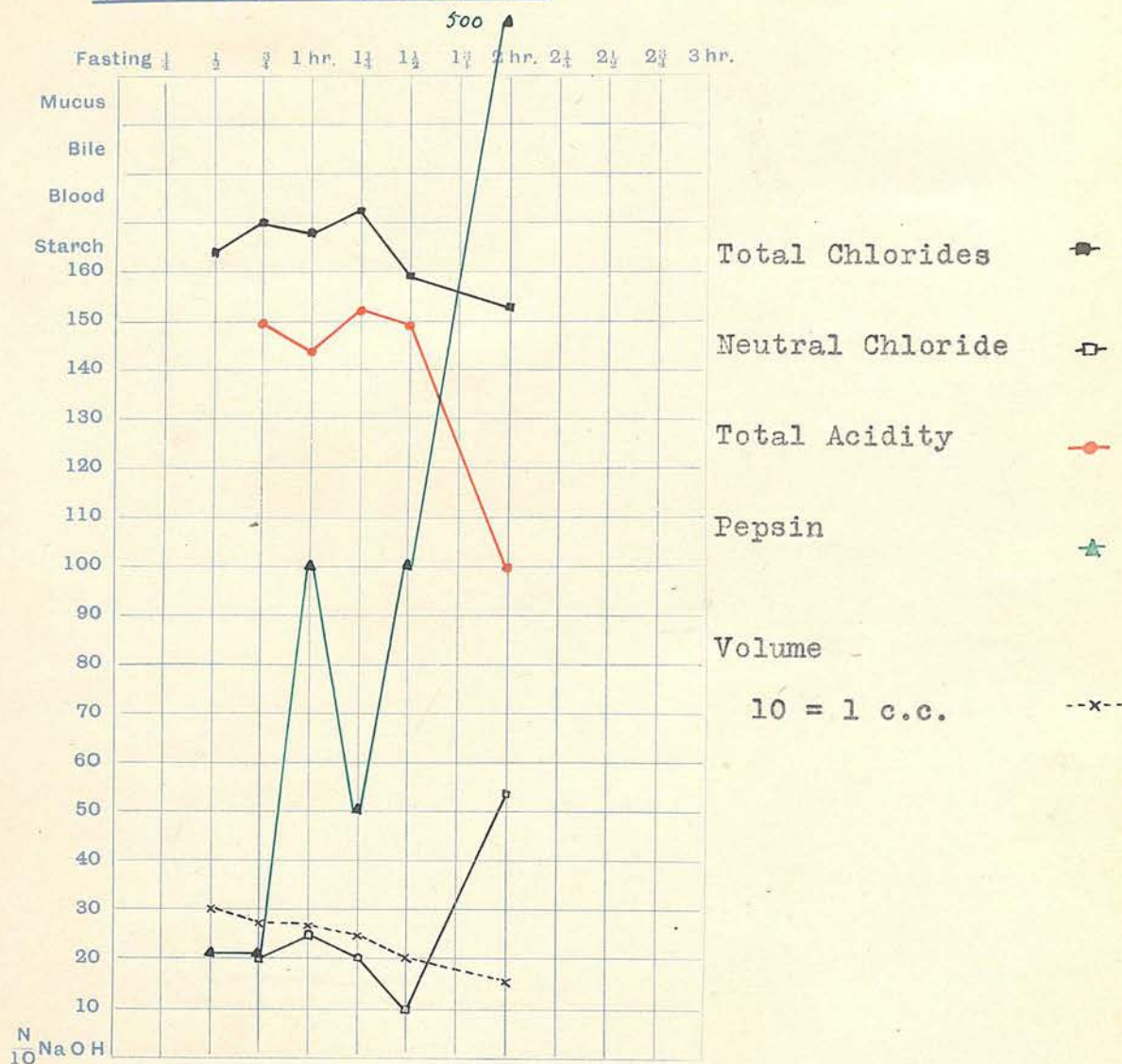
C H A R T S

REPRESENTING PEPSIN-VARIATIONS.

Name of Patient

1. FRACTIONAL TEST-MEAL.

Date 1. 6. '29.



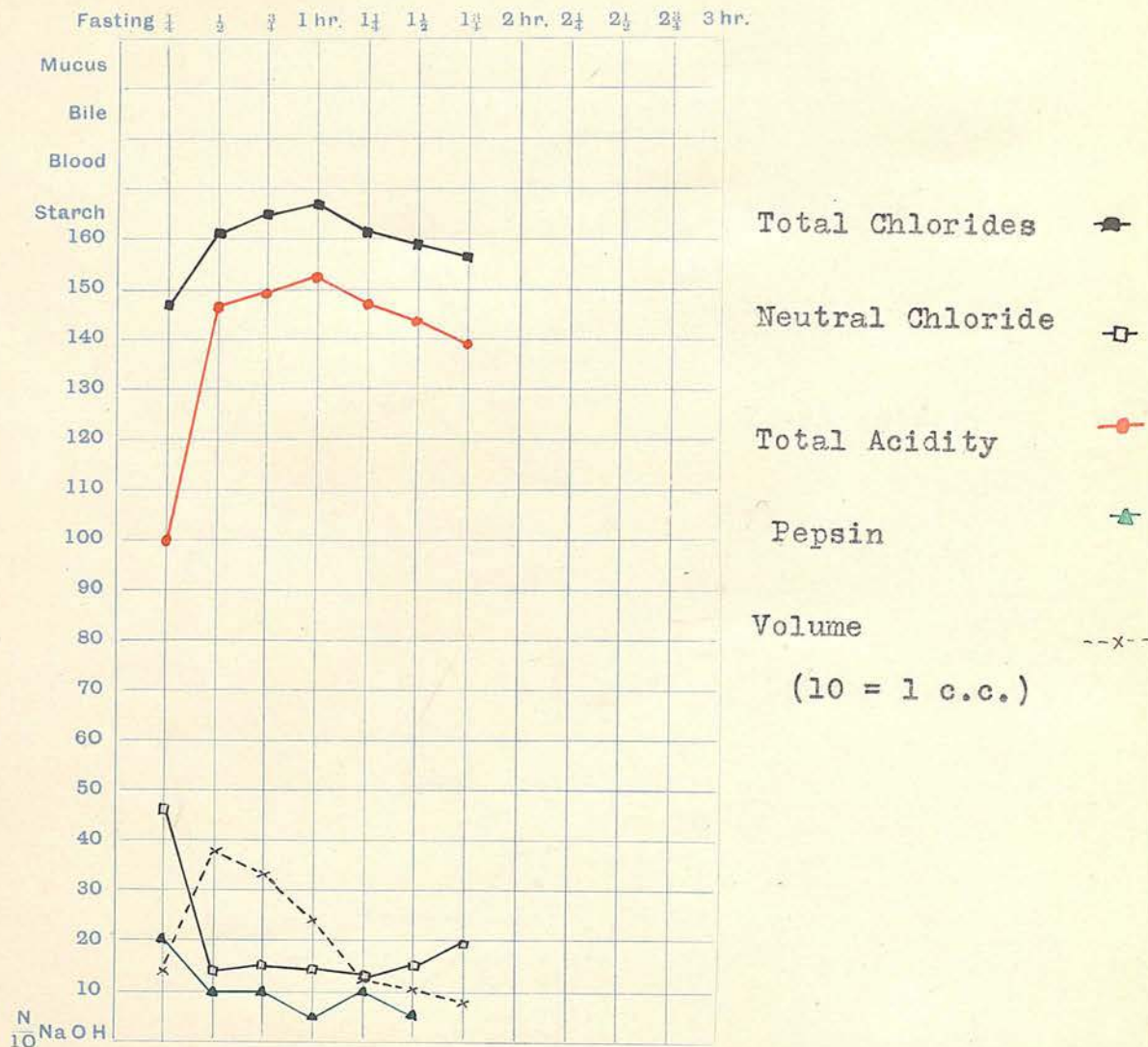
EXPERIMENTAL

100 Gm meat.

Name of Patient

1. FRACTIONAL TEST-MEAL.

Date 4. 6. '29.



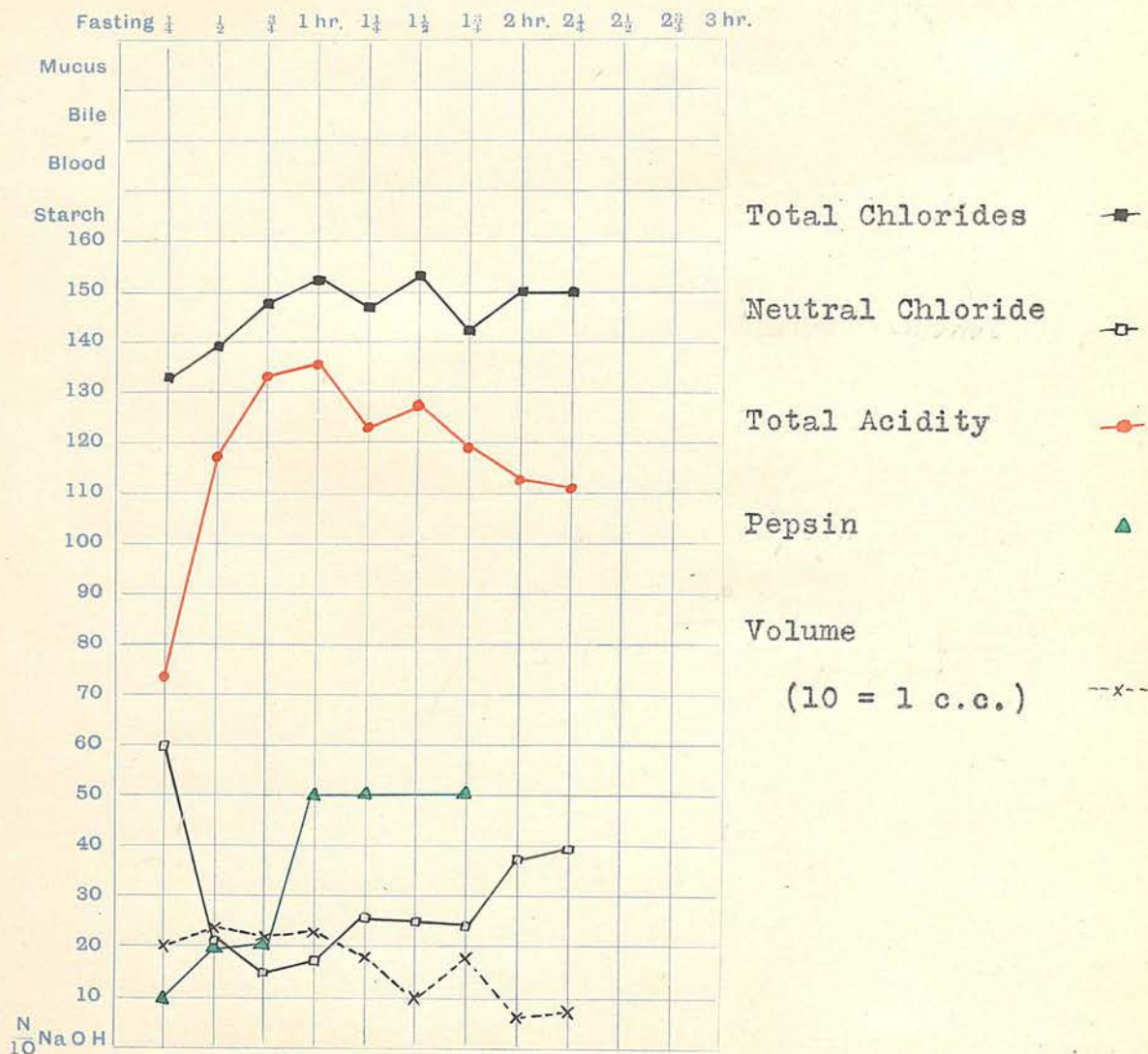
EXPERIMENTAL

300 c.c. Milk.

Name of Patient

1. FRACTIONAL TEST-MEAL.

Date 6. 6. '29.



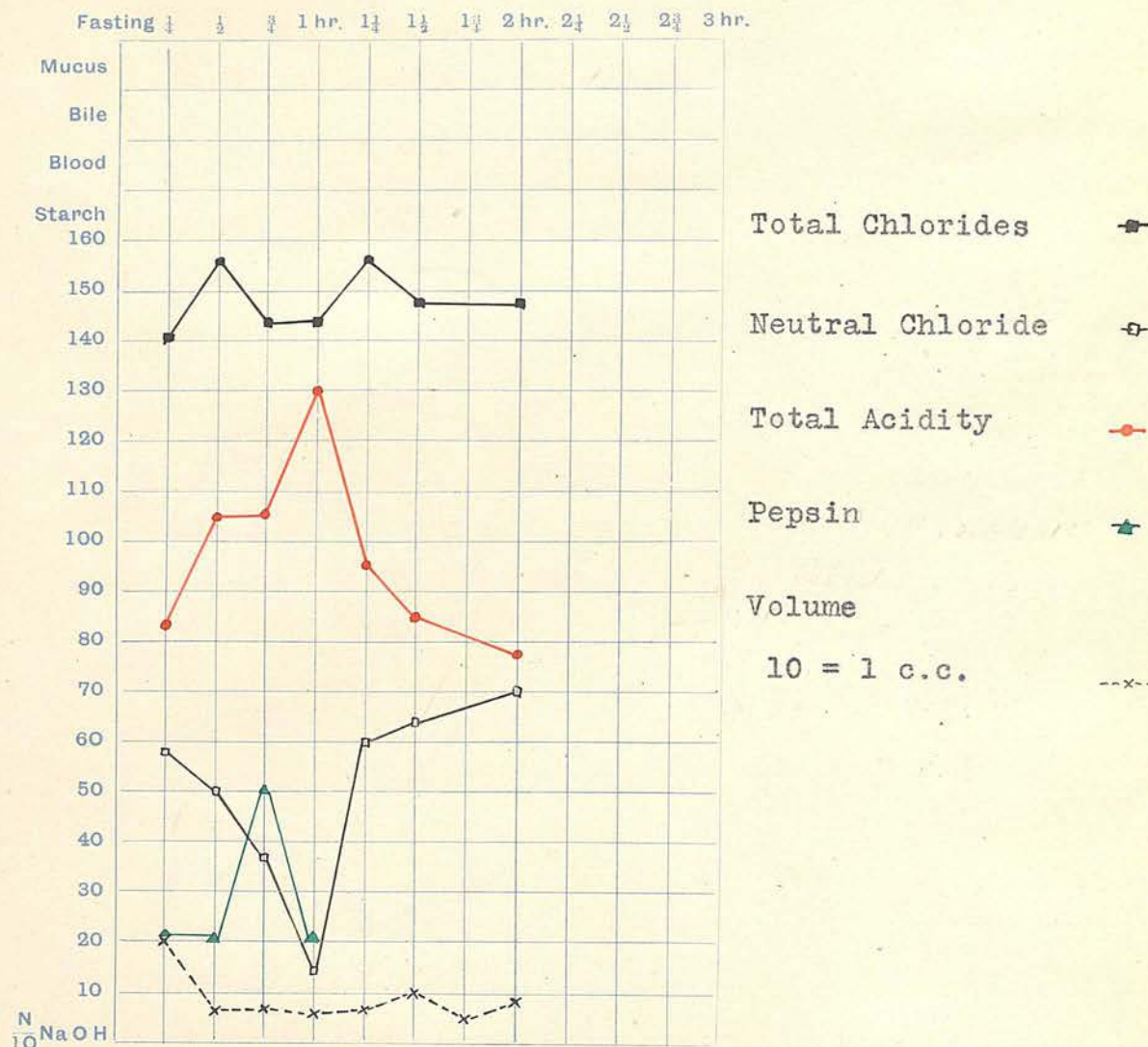
EXPERIMENTAL

75 Gm. Dog biscuit.

Name of Patient

1. FRACTIONAL TEST-MEAL.

Date 7. 6. '29.

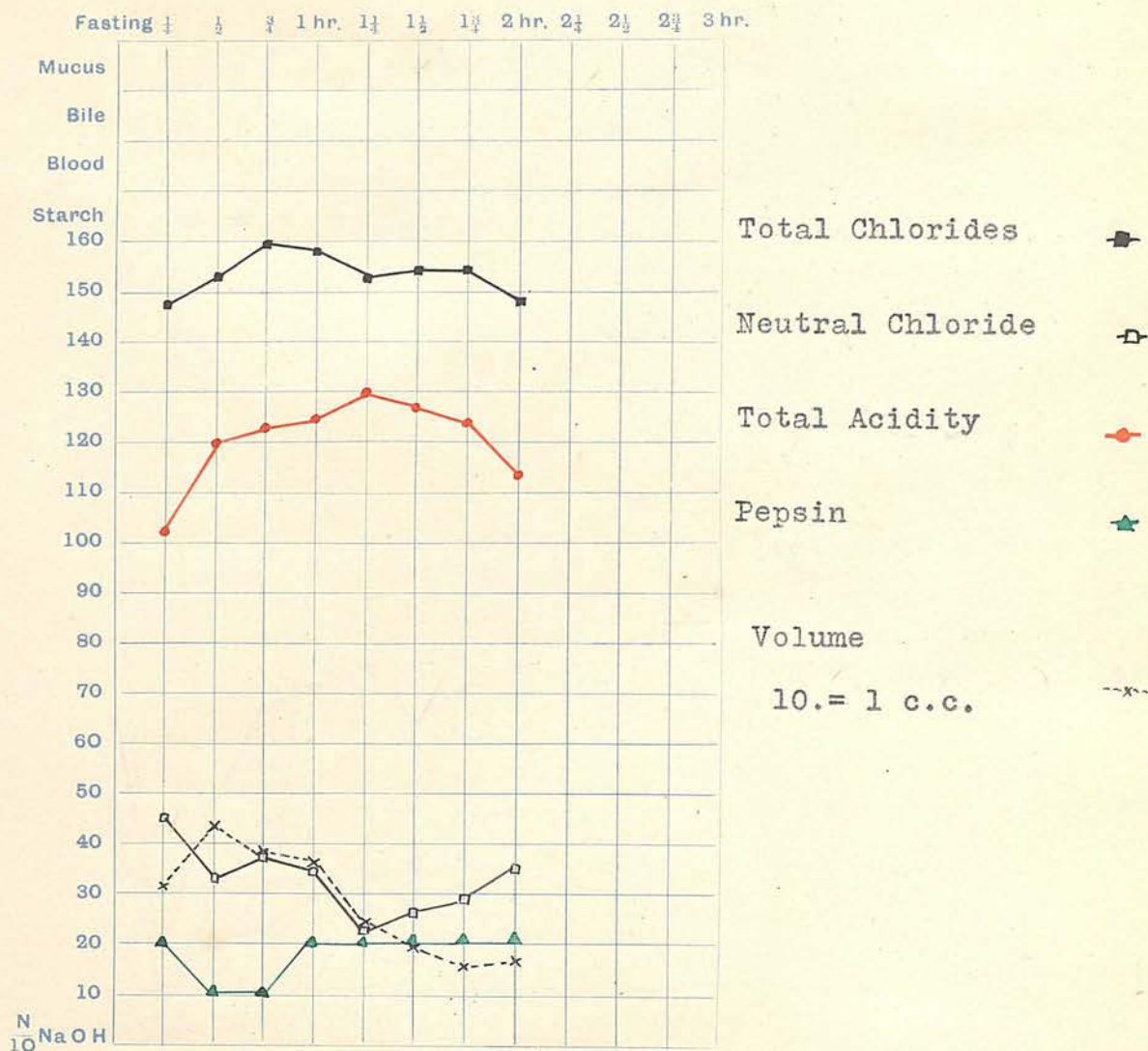


EXPERIMENTAL

65 Gm. Biscuit.

1. FRACTIONAL TEST-MEAL.

Date 8. 6. '29.

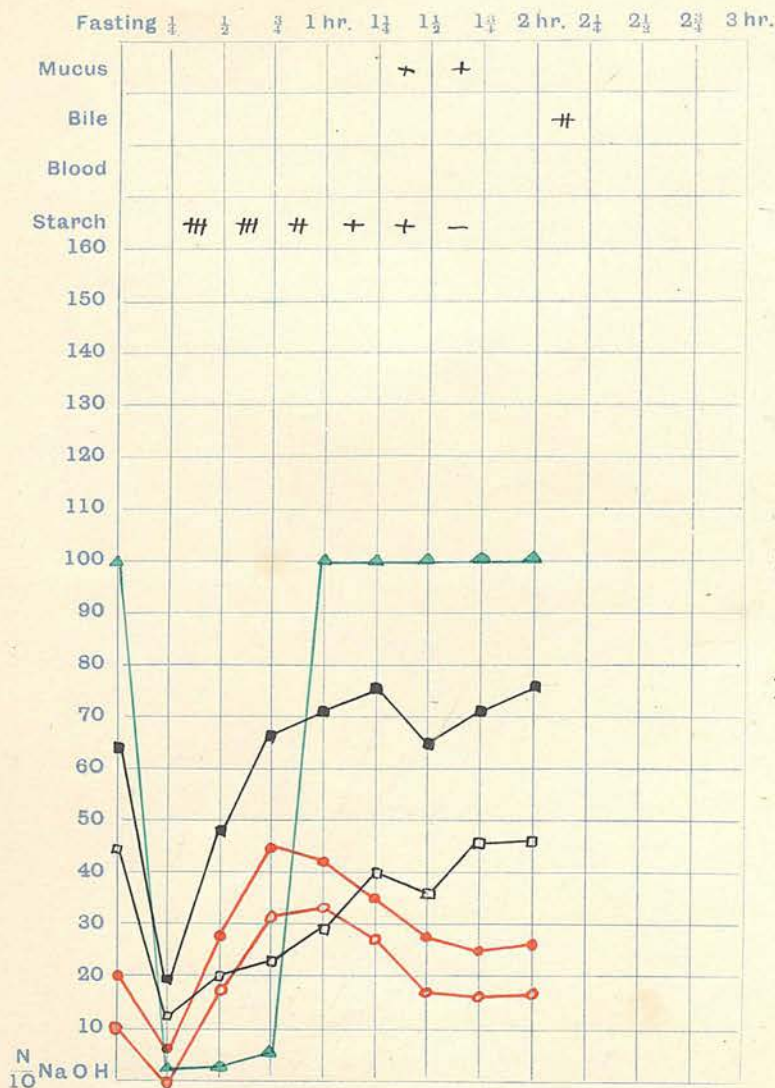


EXPERIMENTAL

200 Gm. equal quantities of
biscuit, meat and milk.

1. FRACTIONAL TEST-MEAL.

Date 21. 6. '29.



Fasting-juice: 15c.c.

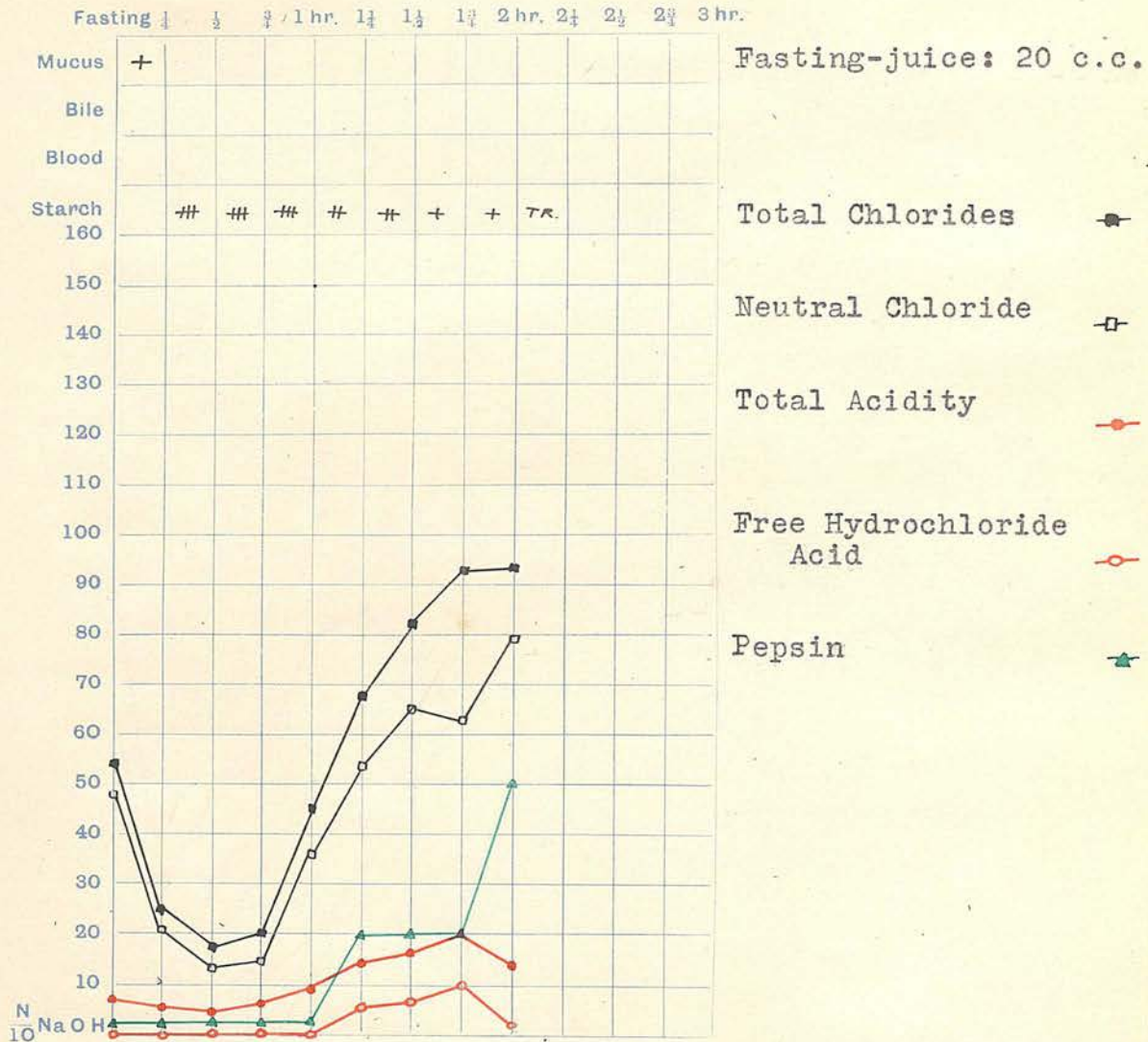
Normal control.

Name of Patient N. 4.

(M. aet. 26)

1. FRACTIONAL TEST-MEAL.

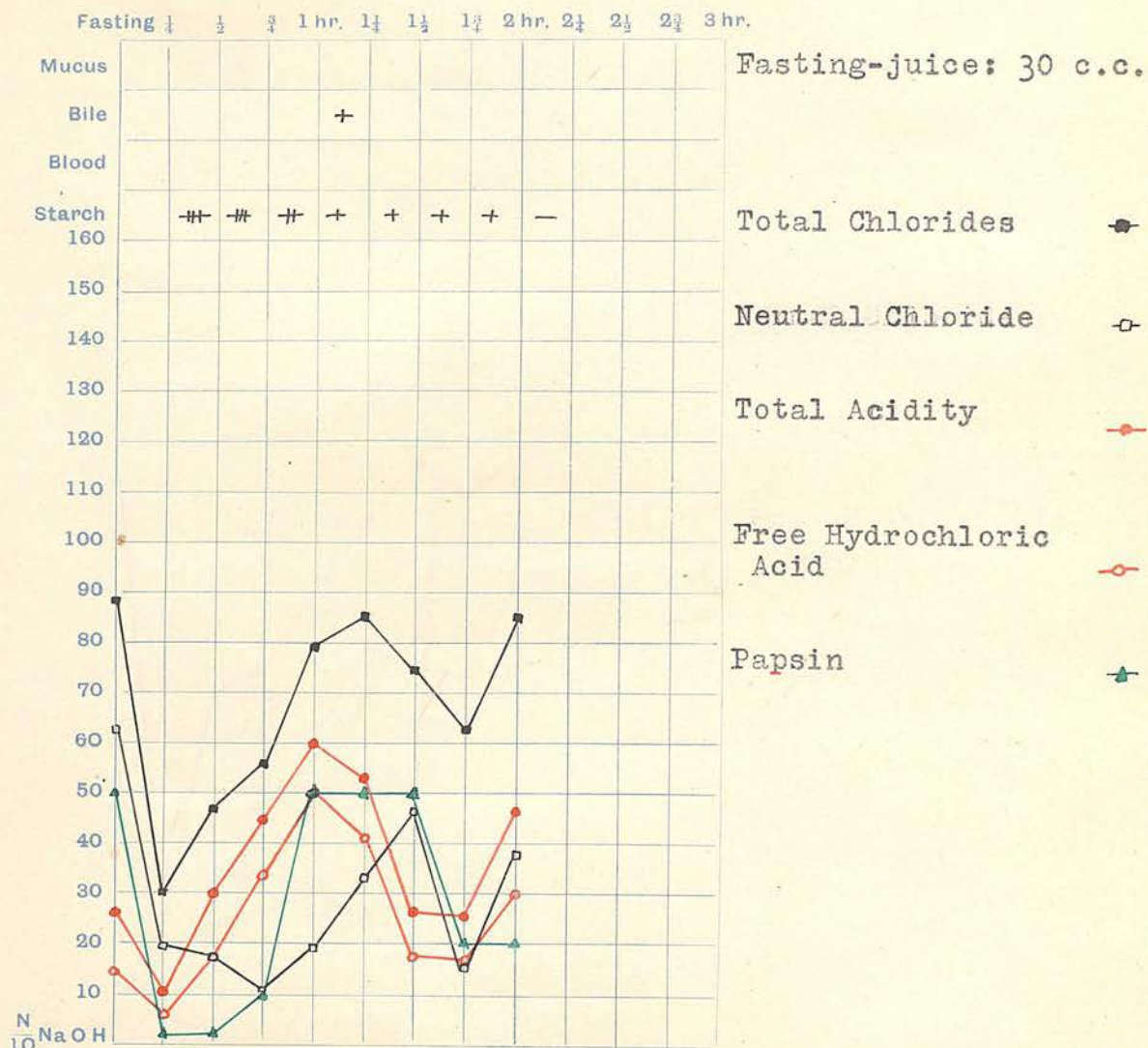
Date 16. 7. '29



Normal Subject.

Name of Patient N. 5. (M. aet. 27)

1. FRACTIONAL TEST-MEAL. Date 16. 7. '29.



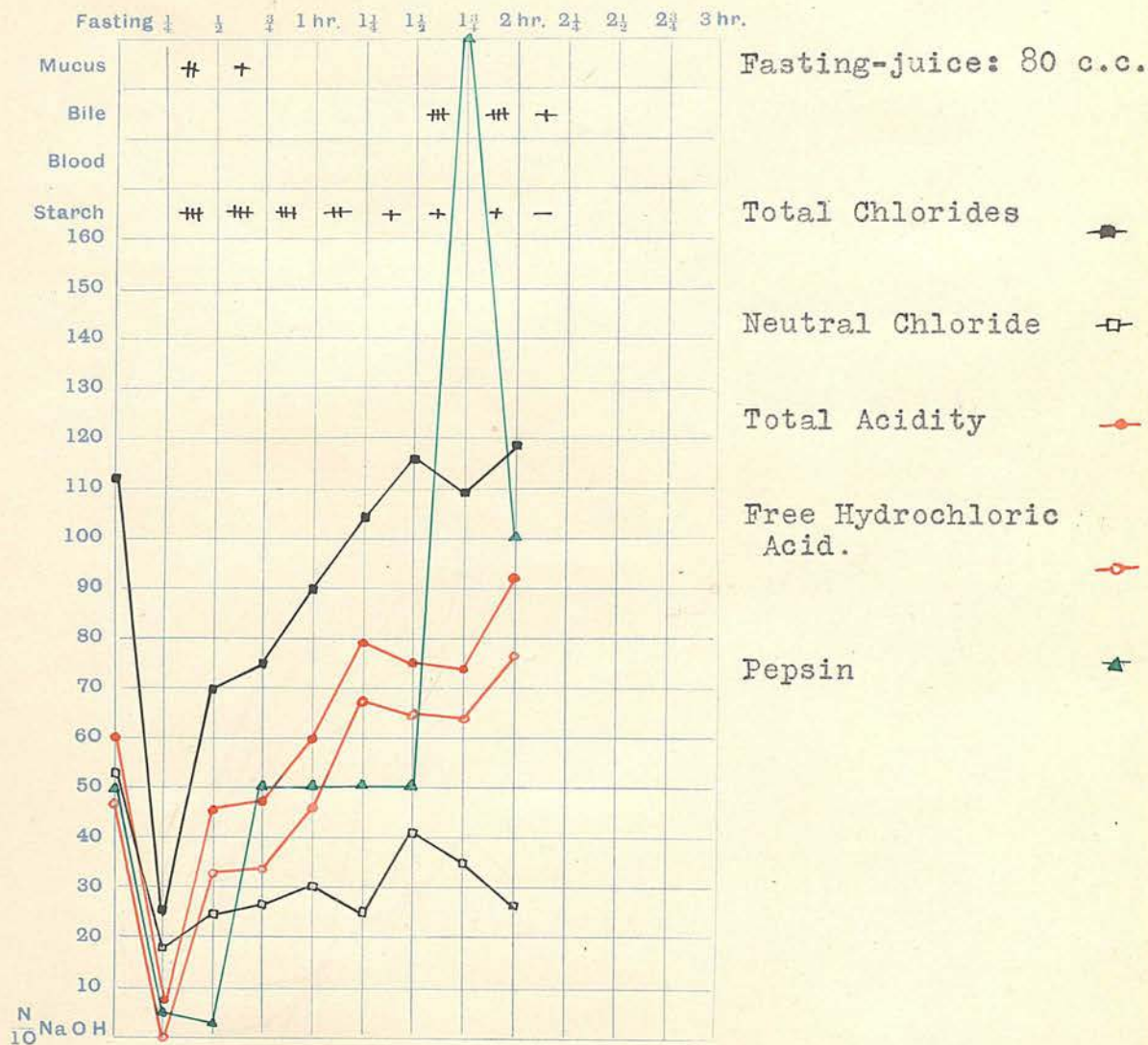
Normal Subject

Name of Patient N. 5.9.

(M. aet. 24.)

1. FRACTIONAL TEST-MEAL.

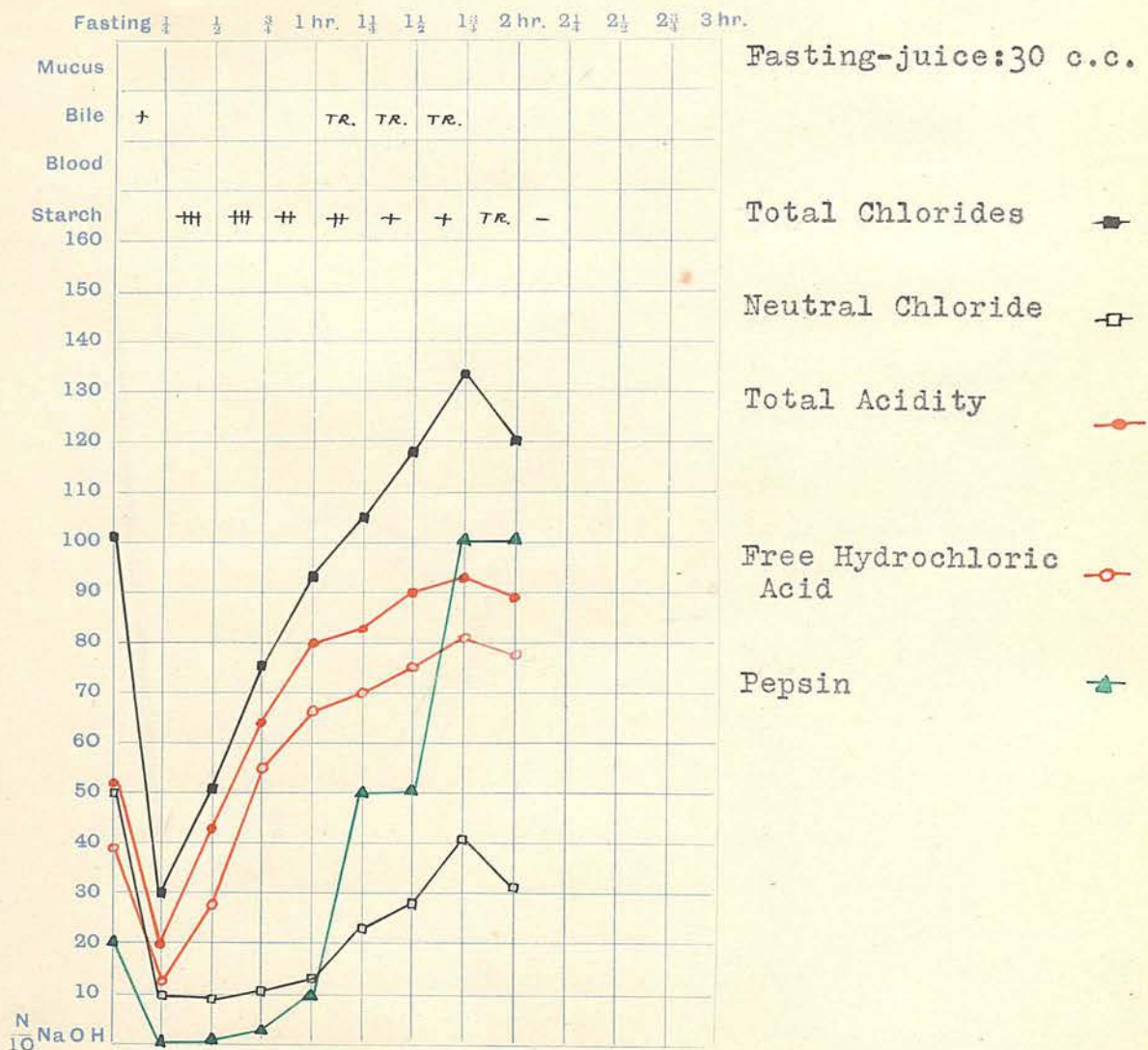
Date 13. 7. '29



Normal Subject

Name of Patient N. 10. (M. aet. 26)

1. FRACTIONAL TEST-MEAL. Date 13. 7. '29.



Normal Subject

Name of Patient

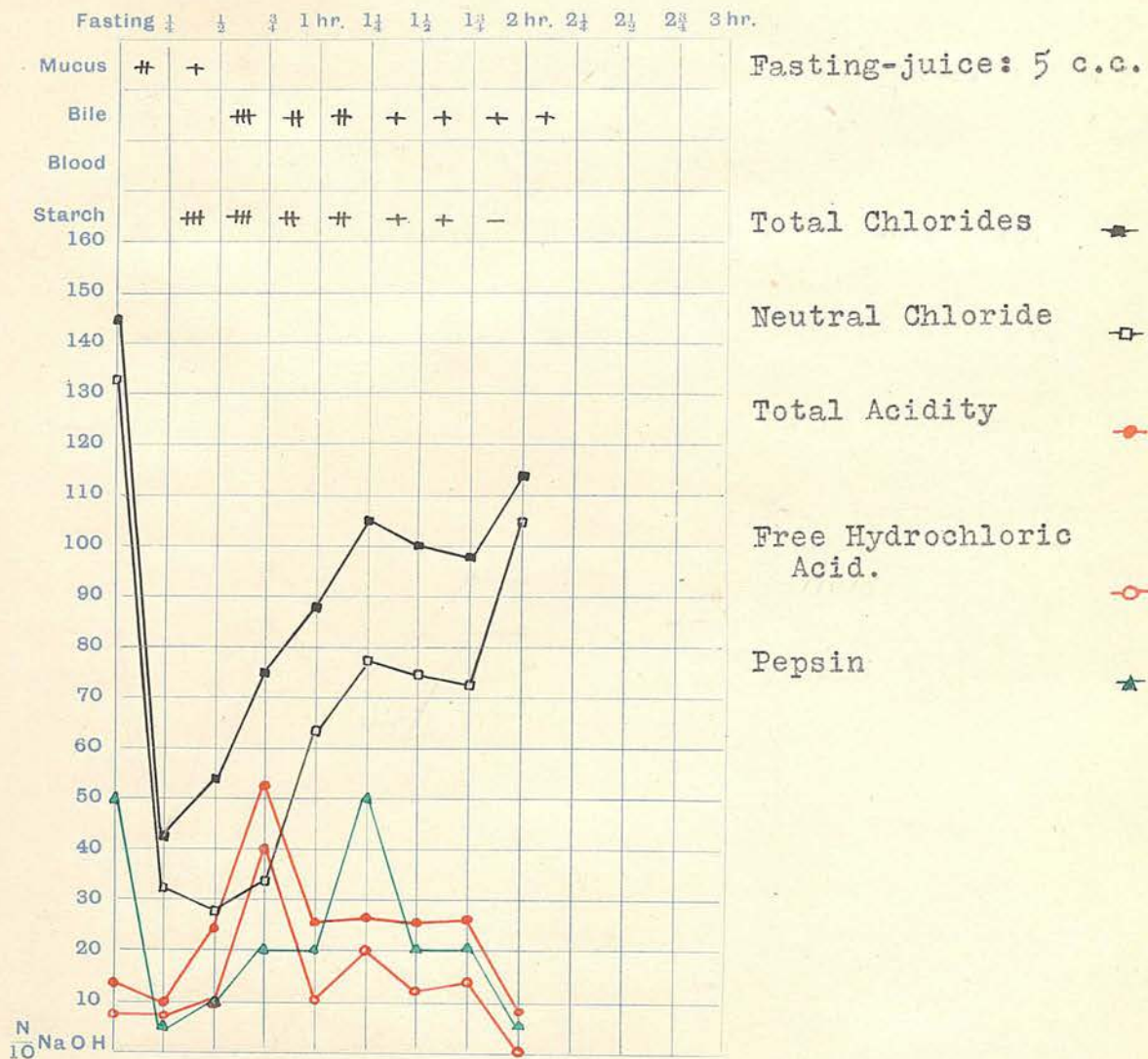
UV

L(C)

(F. aet. 48)

1. FRACTIONAL TEST-MEAL.

Date 29. 8. '29



Gastric ulcer, after gastroenterostomy.

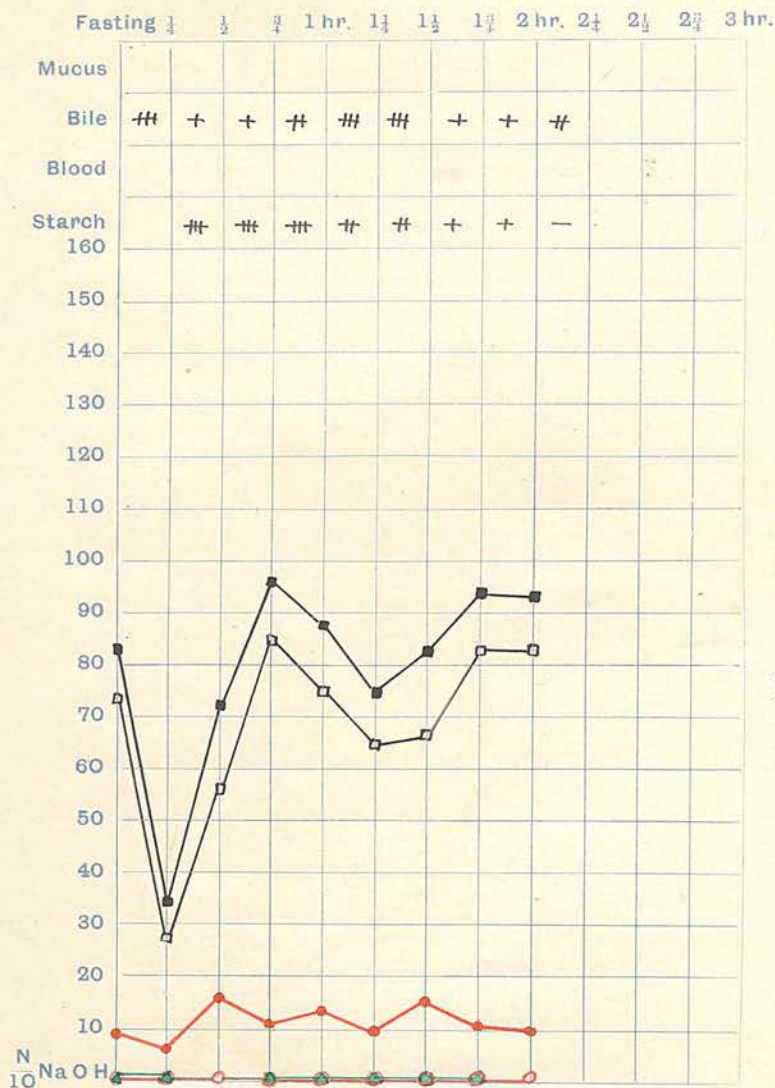
Name of Patient

UV 2 (C)

(M. aet. 37)

1. FRACTIONAL TEST-MEAL.

Date 2. 6. '29



Fasting-juice: 50 c.c.

Total Chlorides

Neutral Chloride

Total Acidity

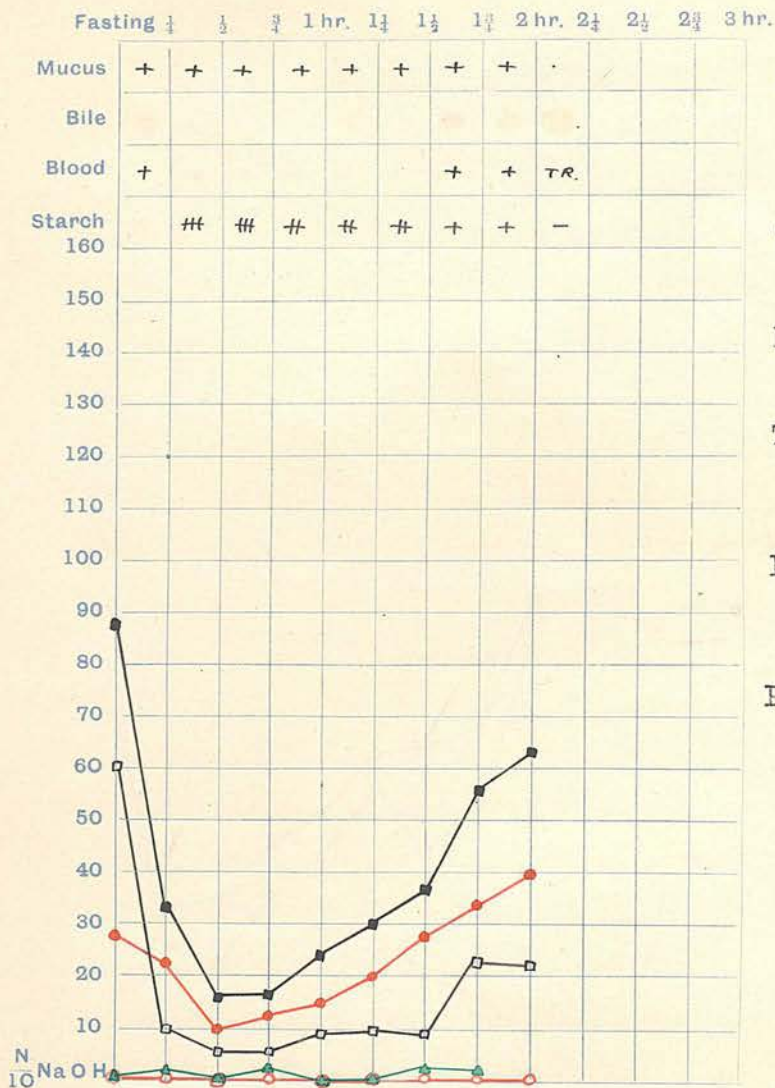
Free Hydrochloric
Acid

Pepsin

Gastric ulcer, after gastroenterostomy.

1. FRACTIONAL TEST-MEAL.

Date 4. 3. '29.



Fasting-juice: 20 c.c.

Total Chlorides

Neutral Chloride

Total Acidity

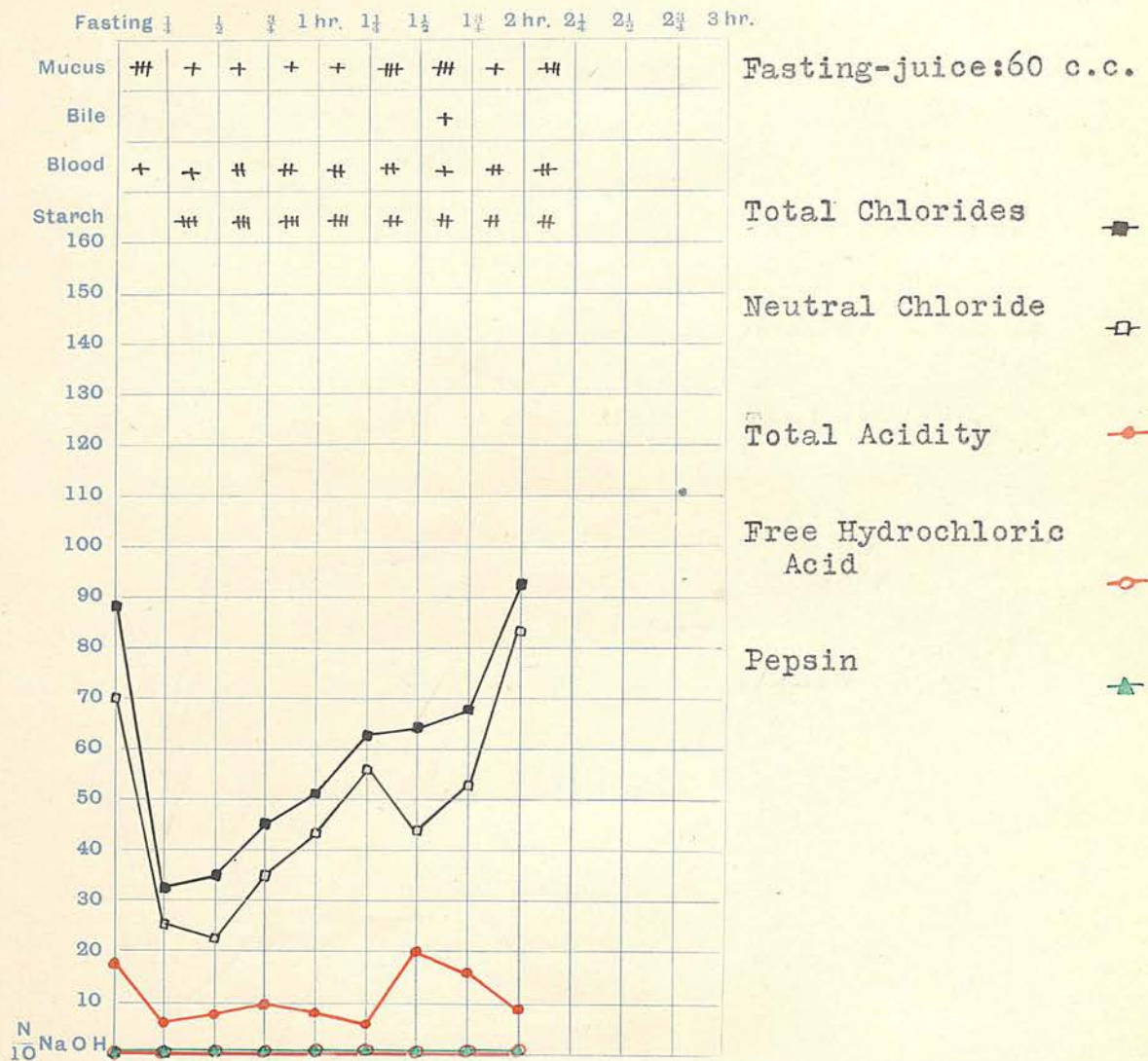
Free Hydrochloric Acid.

Pepsin

Carcinoma of Stomach.

1. FRACTIONAL TEST-MEAL.

Date 29. 5. '29.



Carcinoma of Stomach.

Name of Patient

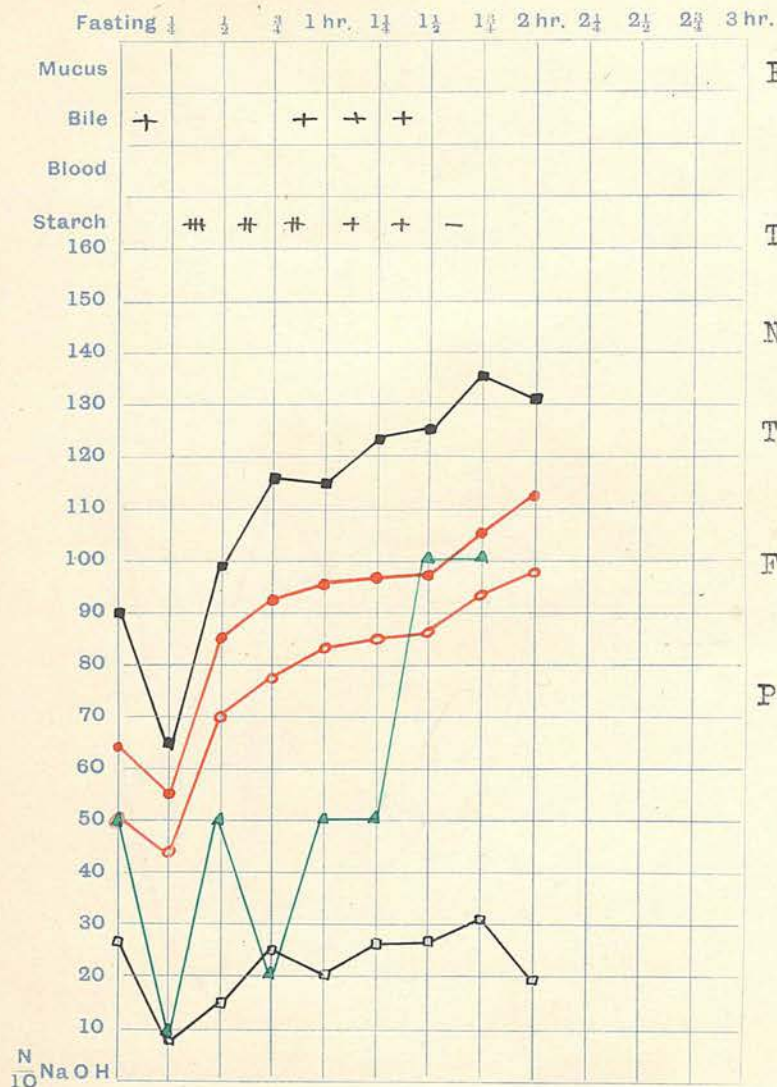
UD 2 (A)

(M. aet. 43)

1. FRACTIONAL TEST-MEAL.

Date

3. 5. '29.



Fasting-juice: 110 c.c.

Total Chlorides

Neutral Chloride

Total Acidity

Free Hydrochloric
Acid.

Pepsin

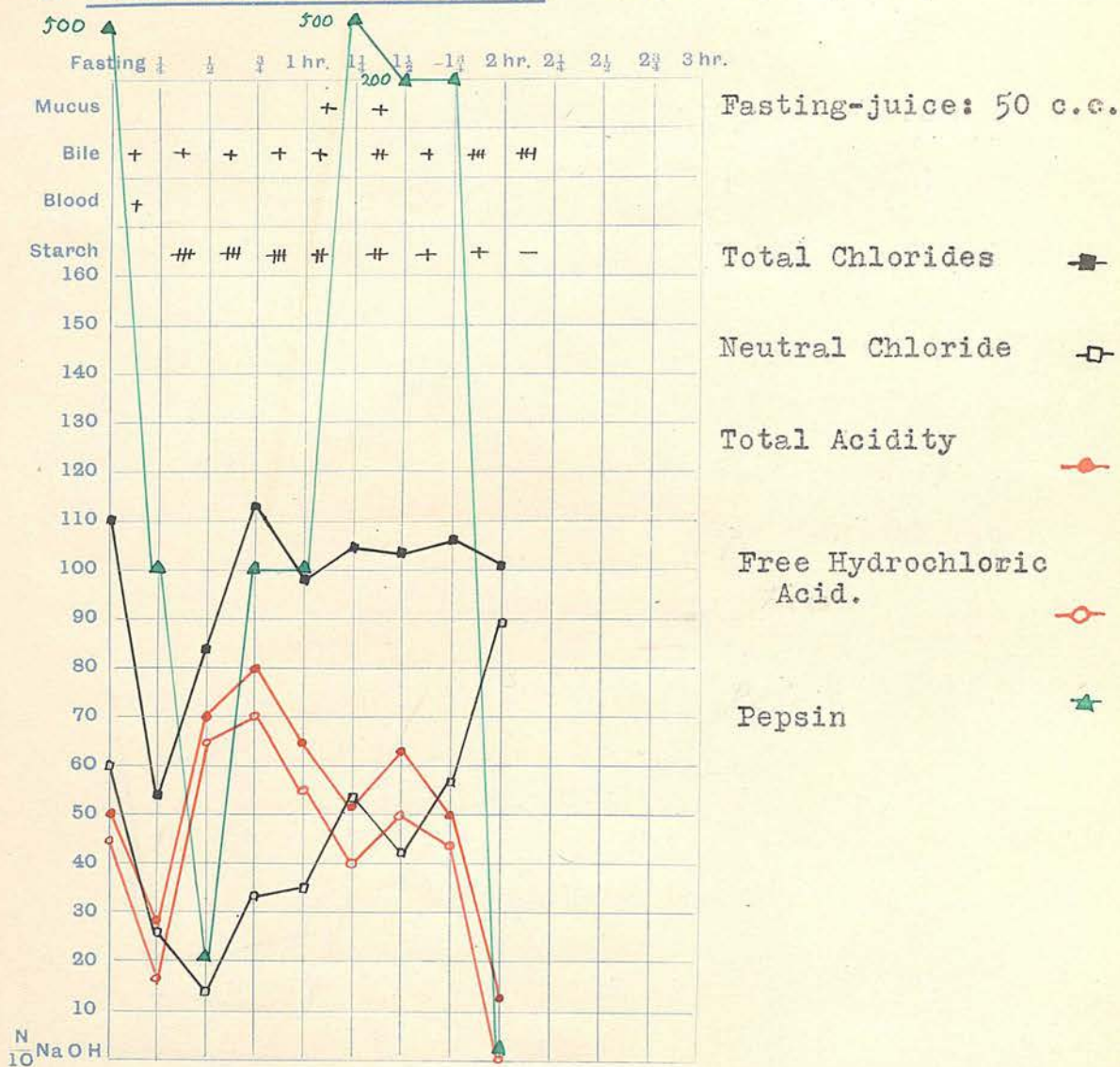
Chronic Duodenal Ulcer: pre-operative.

UD 2 (B)

(M. aet. 48)

1. FRACTIONAL TEST-MEAL.

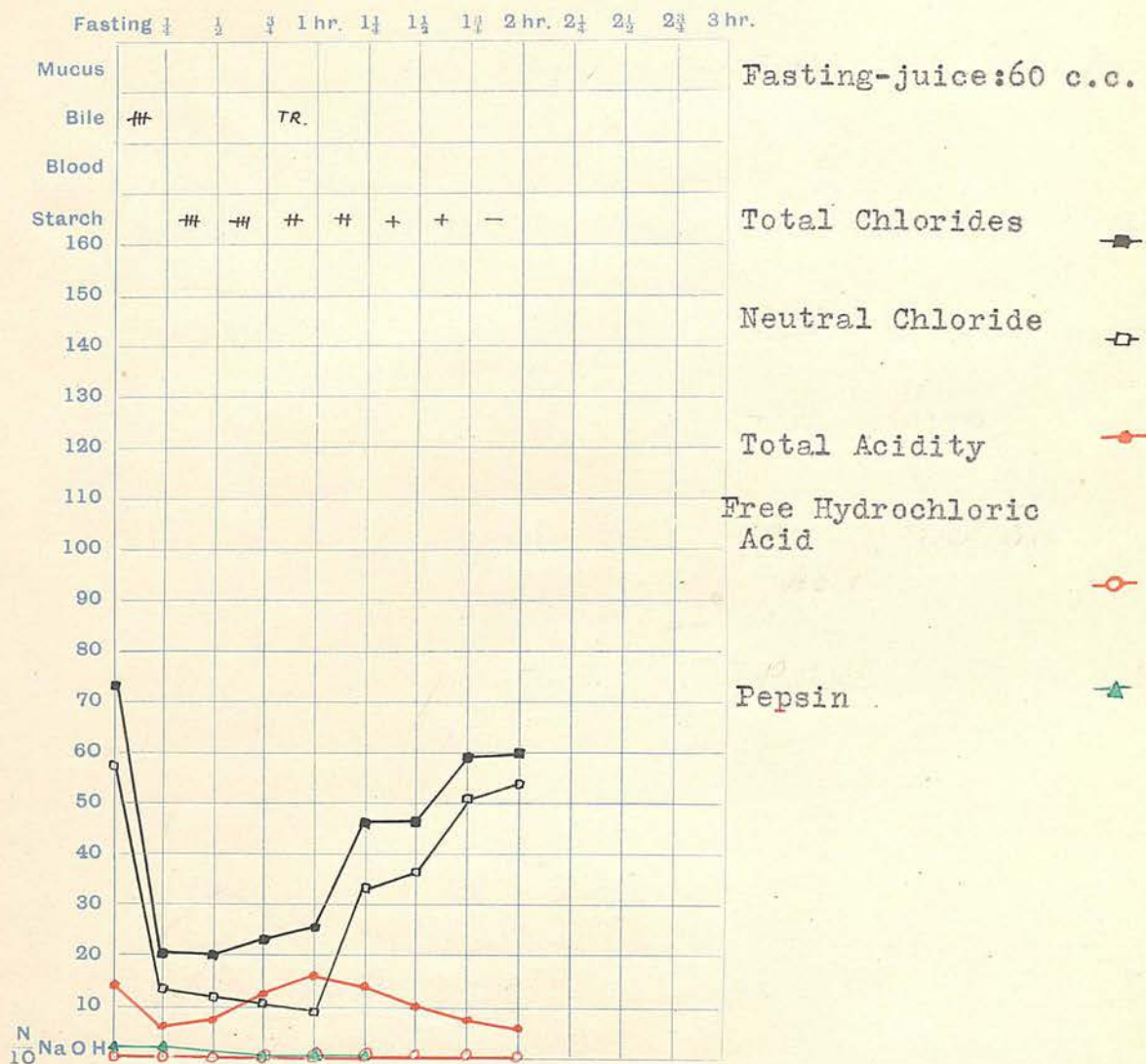
Date 25. 5. '29.



Three weeks after Gastroenterostomy.

Name of Patient P.A. 1 (M, aet. 50)

1. FRACTIONAL TEST-MEAL. Date 26. 6. '29



Pernicious Anaemia.

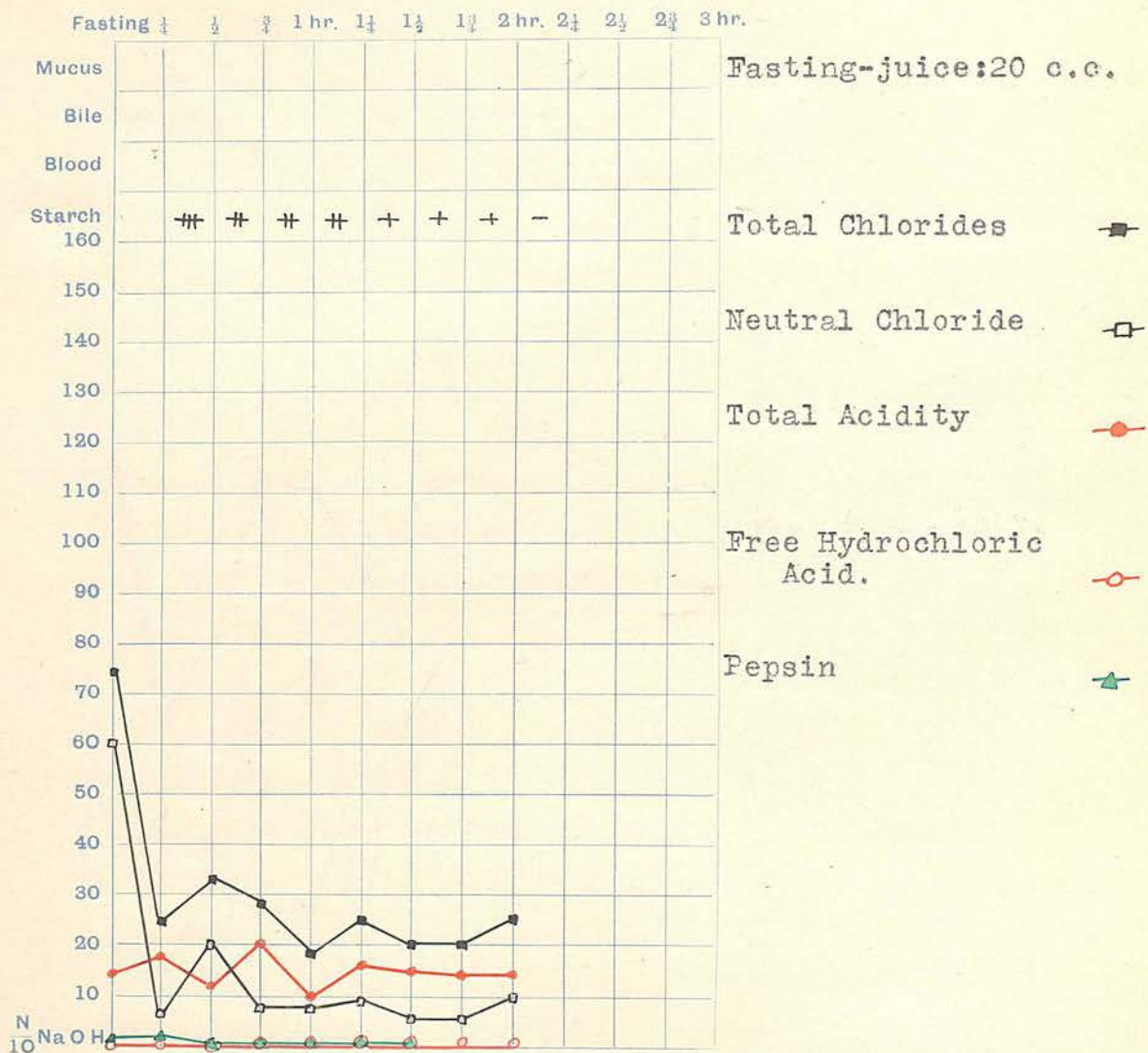
Name of Patient

PA 2.

(M. aet. 46)

1. FRACTIONAL TEST-MEAL.

Date 28. 3. '29.

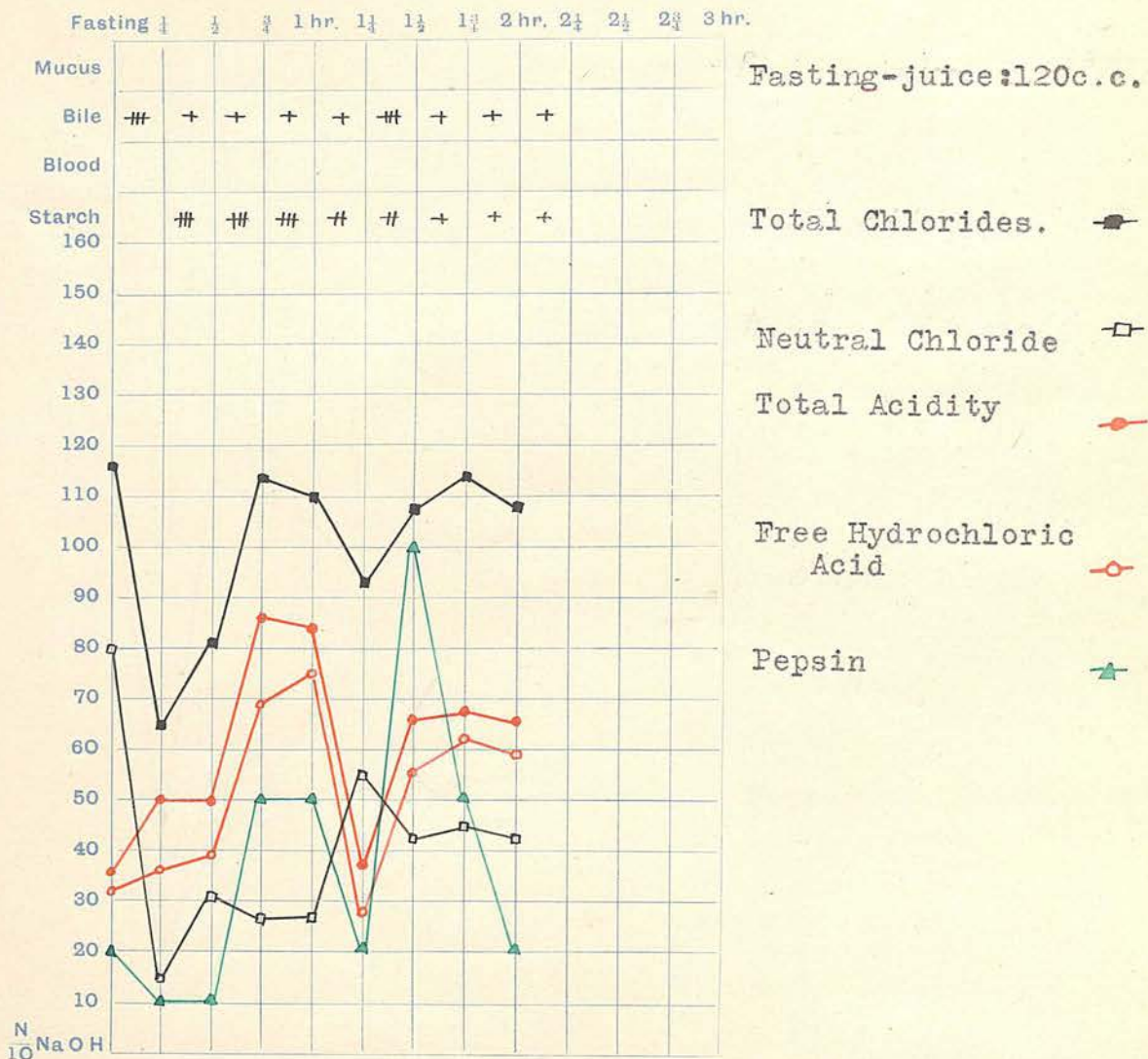


Pernicious Anaemia.

Name of Patient M 1. (M. aet. 30)

1. FRACTIONAL TEST-MEAL.

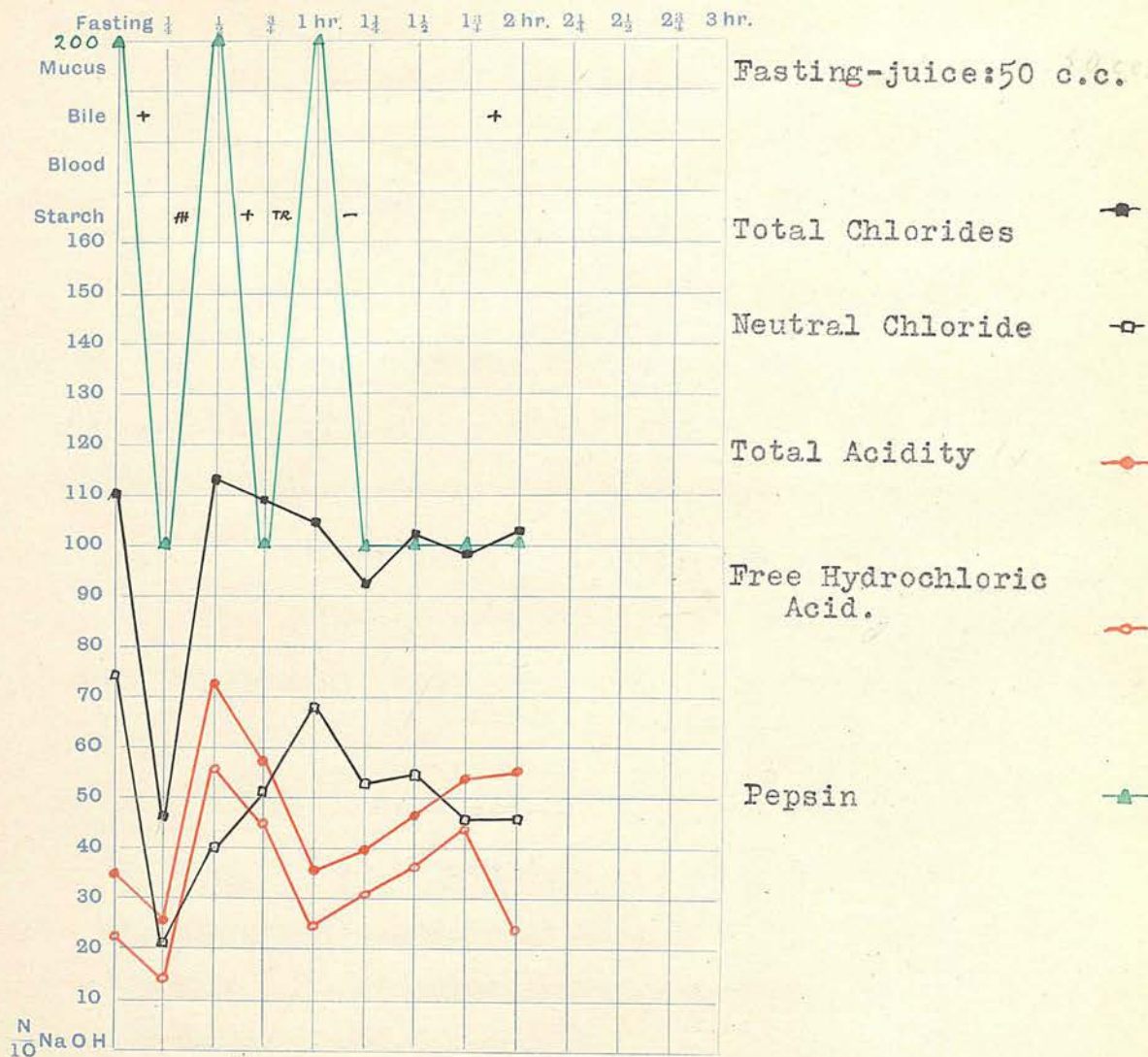
Date 14. 5. '29.



Suspected jejunal ulcer.

Name of Patient M. 2. (M. aet. 38)

1. FRACTIONAL TEST-MEAL. Date 20. 5. '29



Multiple tuberculous structures of
Small Intestine.

DISCUSSION OF RESULTS.

(A) EXPERIMENTAL RESULTS.

A definite proteolytic action in the secretion of the lower half of the fundus was noted. No marked variation of pepsin-concentration was seen during the period of observation - two hours. No close relation between peptic-activity and acidity was found. The juice of greatest digestive power was secreted on meat, next on biscuit, and least on milk.

For equal amounts of the different foods, employed, most secretion was obtained with dog-biscuit, less with meat, and least with milk.

(53)
PAVLOV, classified the foodstuffs according to their nitrogen content, and calculated the amounts of each which contain the same quantity of nitrogen. 'Ferment-units', so-called, were obtained by multiplying the volume of the juice by its digestive power (calculated by METTE'S Method). He found that for a definite nitrogen content most 'units' were secreted on bread, (1600), less on meat (430) and least on milk (340).

The writer found corresponding values for the secretion of the 'low' fundus pouch: in the case of dog-biscuit 1500 'units', meat 660 'units' milk 520 'units'. The dog biscuit used in these experiments/

experiments contained ground, dried flesh, baked with coarse flour; it was probably more easily disintegrated than the bread employed by PAVLOV, and its nitrogen content was approximately double.

B. CLINICAL RESULTS.

Practical estimations, by the new method, were performed in fifteen individuals, including both normal and pathological cases.

In all but one, pepsin was present at some time during the investigations; in the exception, (CV3), owing to the small volume of the samples obtained, estimations on the undiluted contents could not be carried out.

NORMAL SERIES.

Pepsin was found at some time in every case. The average concentration was highest in N 1. and lowest in N 4. No quantitative relation could be established with any other constituent of the secretion; this is in agreement with the view of LIM,⁽⁴¹⁾ MATHESON & SCHLAPP⁽⁴²⁾, and LOEPER & BAUMANN, using the methods of HATA and HAMMERSCHLAG respectively.

The/

The curve of concentration usually showed a fall immediately following the ingestion of the meal, rising later, as noted by EHRENREICH⁽¹⁹⁾,
 DELHOUGNE⁽¹⁶⁾, however, using the nephelometric method, described a terminal fall.

The contour of the curve most resembled that of the total chlorides; this agrees with the conclusions of BUTCHER⁽¹³⁾, with the original METTE^{*} method.

GASTRIC and DUODENAL ULCER.

No obvious increase in pepsin-concentration was noted, confirming the findings of FRANKE⁽²¹⁾, with BOAS' test. The opposite view is held by OPPLER⁽⁵⁰⁾, from the results of his own technique, by MANASSE⁽⁴⁶⁾, employing the method of FULD & LEVISON, and by DELHOUGNE.

No post-operative results are available for comparison. In one case of duodenal ulcer in the series, (UD2), gastroenterostomy with partial reduction of acidity, was followed by a striking increase in the average enzyme-concentration of the specimens; an abrupt terminal fall was here noted, coinciding with the disappearance of free hydrochloric acid.

In/

In a case of gastric ulcer, (UV2), the establishment of achlorhydria was accompanied by the almost complete disappearance of peptic activity. In a second case, (UV1) where free acidity had been reduced, although not abolished by operation, the pepsin curve was low.

CARCINOMA of the STOMACH.

In the case, (CV3), as already explained, the undiluted contents were not examined; no precipitation was observed in the lowest dilutions; in another case there was evidence of very weak peptic activity. This confirms the statements of HIRSCH-MAMROTH & RINDFLEISCH⁽³⁴⁾, from the results of BOAS' method, and of MANASSE, although the latter has detected a high concentration of pepsin in the contents from one case of carcinoma of the stomach.

Blood in the gastric contents has been stated by HIRSCH-MAMROTH & RINDFLEISCH to inhibit completely peptic digestion. This was not found to be so in the case of CV 2. Similarly, MANASSE reports evidence of peptic activity in the presence of blood.

PERNICIOUS/

PERNICIOUS ANAEMIA.

In two cases examined, minimal concentrations of enzyme were observed.

In general, the writer finds that achlorhydria or a low free acidity is accompanied by a low pepsine-concentration. With increase of acidity this relationship apparently disappears; OPPLER, MANASSE, HIRSCH-MAMROTH and RINDFLEISCH, however, state that there is a parallelism between acidity and peptic activity.

No definite conclusion can from these investigations be drawn as to the diagnostic value of the method, but its chief importance seems to lie in its application to the differential diagnosis of ulcer from carcinoma of the stomach. So far as is known, it does not enable a distinction to be drawn between the varieties of achlorhydria.

SUMMARY/

S U M M A R Y.

The concentration-variations of chlorides, acid and pepsin, in gastric contents, have been studied.

One hundred investigations of chlorides and acid alone, and fifteen of pepsin were carried out in both normal and pathological cases. Estimations of these constituents were also performed on the secretion obtained from an isolated pouch, with nervous connections intact, constructed in the lower half of the fundus of a dog's stomach.

CONCLUSIONS/

CONCLUSIONS.

- I. The chief diagnostic value of estimations of the chlorides, in addition to that of the acid, lies in assisting differentiation of such pathological conditions of the stomach as are characterised by complete absence of 'free' hydrochloric acid.
 - II. The determination of pepsin-variations seems to be of most service in distinguishing between Carcinoma of the Stomach and Gastric or Duodenal Ulcer.
 - III. The mechanism of control of gastric acidity is dependent upon several contributory factors.
The suggestion is made that the gland-cells of the pyloric segment of the stomach represent the principal source of secreted neutral chloride.
-

B I B L I O G R A P H Y .

1. ACKERMANN, J.H., "Experimentelle Beiträge zur Kenntniss des Pylorussecretes beim Hunde". Skandin. Arch.f.Physiol., Leipzig, 1894. 5:134-49.
2. BAIRD, M.M., CAMPBELL, M.H., & HERN, J.R.B., "The Importance of Estimating Chlorides in the Fractional Test Meal Samples, and some Experiments with the Duodenal Tube". Guy's Hosp.Rep., 1924. 74: 23-54.
3. BEAUMONT W., "Experiments and Observations on the Gastric Juice and the Physiology of Digestion". Plattsburgh, 1833.
4. BEAUMONT, G.E., & DODDS, E.C., "Recent Advances in Medicine". 3rd ed. Lond., 1926.
5. BOAS, I., "Eine neue Methode der Pepsinbestimmung in Mageninhalt". Deut.Med.Woch., 1925. 51: 511-12.
6. BOLDIREV, W., "Der Uebertritt des natürlichen Gemisches aus Pankreassaft, Darmsaft und Galle in den Magen. Pflüg. Archiv. 1907, CXXI. 13-53.
7. BOLDIREV, W. "The Self-regulation of the Acidity of the Gastric Contents, and the Real Acidity of the Gastric Juice". Quart.Journ.Exp.Physiol. 1914-15, 8: 1-12.
8. BOLTON, C., "The interpretation of Gastric Symptoms". Lancet 1928, 1: 1263-75.
9. BOLTON, C., & GOODHART, G.W., "Duodenal Regurgitation into the stomach during Gastric Digestion". Lancet 1922. 1:420-25
10. BOLTON, C., Diseases of the stomach with special reference to modern methods of investigation. Brit.Med.Journ.1923, 2. 269-74.
11. BOLTON, C., & SALMOND, R.W.A., "Antiperistalsis of the Duodenum and its Relation to Pyloric Regurgitation". Lancet, 1927. 1. 1230-32.

II.

12. BRUCKE, E., Beiträge zur Lehre von der Verdauung Sitzungsber.d.k.Akad.d.Wissensch. Wien, 1859, 37: 131. (Quoted by E.A. Schäfer, 'Text Book of Physiology' 1898)
13. BUTCHER, T.A., "Observations on the Gastric Acidity and Secretion in Health". Quart. Journ. Med. 1925, 19: 455-78.
14. CATHCART, E. P., "Reflux from Intestine to Stomach". Journ. Physiol. 1911, 42: 433-38.
15. CITRON, H., "Ueber quantitative Pepsinbestimmung im Magensaft". Deut.Med.Woch. 1926. 52: 1781-82.
16. DELHOUGNE, F., "Untersuchungen ueber den Pepsingehalt des Magensaftes". Deut.Arch. f.Klin.Med. 1927. 157: 299-308.
17. DUNN, HALBERT L., "Application of Statistical Methods in Physiology". Phys.Rev.1929 9: 275-398.
18. DUTHIE, R.J., "Variation of Free Hydrochloric Acid and Total Chloride in the Upper and Lower Parts of the Stomach". Quart.Journ.Med. 1928-29.XXII:575-80.
19. EHRENREICH, M., Ueber die Kontinuierliche Untersuchung des Verdauungsablaufs mittels der Magenverweilsonde, Zeitschr. f.Klin.Med. 1912. 75: 231-52.
20. FISHER, R.A., Statistical Methods for Research Workers". Edinburgh, 1925.
21. FRANKE, K.F., "Ueber Pepsinbestimmungen mit der Methode von Boas, speziell nach Alcoholprobefrühstück". Deut.Med.Woch. 1927, 53: 275-76.
22. FULD, E., & LEVISON, L.A., "Die Pepsinbestimmung mittels der Edestinprobe", Biochem.Zeitschr. 1907, 6: 473-501.

III.

23. GAMBLE, J.L., & McIVER, M.A., "Fixed Base in Gastric Juice". Proc.Soc.Exper.Biol. & Med. 1926. 23: 439-43.
24. GAMBLE, J.L., & McIVER, M.A., "The Acid-base Composition of Gastric Secretions". Journ.Exper.Med. 1928. 48: 837-47.
25. GRAHAM, G.A., "A Study of the Alterations of the Hydrochloric Acid in the Gastric Juice, due to Carcinoma of the Stomach". Quart.Journ.Med., 1910-11, 4:315-35.
26. GRÜTZNER, P., "Ueber eine neue Methode Pepsin mengen zu bestimmen". Pflüg. Archiv. 1874, 8: 452-59.
27. HAMMERSCHLAG, "Quoted by REHFUSS, M.E., (58).
28. HANSMAN, F.S., DAY, E.M., & CLIFTON, R., "Gastric Chlorides, Their Origin & Significance". Med. Journ.Austral. 1927. 2: 6-13.
29. HATA, "Quoted by LIM, MATHESON & SCHLAPP, (41).
30. HEIDENHAIN, R., "Ueber die Pepsinbildung in den Pylorusdrüsen". Pflüg.Archiv. 1878.18: 169-71.
31. HEIDENHAIN, R., "Ueber die Absonderung der Fundusdrüsen des Magens." Pflug.Archiv. 1879, 19: 148-66
32. HEILMEYER, L., "Klinische Beiträge zur Physiologie und Pathologie der Magensekretion". Deut.Archiv.f.Klin.Med., 1895. 148: 273-312.
33. HICKS, C.S., & VISHNER, J.W., "The Mechanism of Regurgitation of Duodenal Contents into the Stomach". Am.Journ.Physiol. 1915. 39: 1-8.
34. HIRSCH-MAMROTH, P., & RINDFLEISCH, H., (Quoted by HIRSCHBERG, F., Archiv f.Verdaunungs-kr.1928. 43: 211.) Ergebnisse der Magensaftuntersuchung mit der neuen Pepsinbestimmungen nach Boas. Deut.Med. Woch. 1925. 51: 512-13

35. IVY, A.C., & OYAMA, Y., "Studies on the Secretion of the Pars Pylorica Gastri." Amer.Journ.Physiol., 1921, 57:51-60.
36. JUSTESEN, TH., "Ueber den Einfluss verschiedener Nahrung auf die Salzsauresecretion und den Osmotischen Druck im normalen menschlichen Magen". Zeitschr.f.Klin. Med., 1901. 42:451-69.
37. KAMENSKY, Trans.Soc.Russ.Physicians, St.Petersburg, lxi. 243 (Quoted by BOLDIREV (7))
38. KLEMENSIEWICZ, R., "Ueber die Succus Pyloricus" Wien.Akad.Sitzungsber.lxxi, 1875. (Abth 3) pp.249-296.
39. LANGLEY, J., & SEWALL, "Changes in Pepsin-forming Glands during Secretion, Journ. Physiol. 1879 2:281-301.
40. LIM, R.K.S., & DOTT, M.M., "Observations on the Isolated Pyloric Segment and on its Secretion". Quart.Journ.Exp.Physiol., 1922-23. 13:159-76.
41. LIM, R.K.S., MATHESON, A.R., & SCHLAPP, W., "Observations on the Human Gastroduodenal Secretions, with special reference to the Action of Histamine". Quart.Journ.Exper.Physiol. 1922-3. 13:361-78.
42. LOEPER, M. et BAUMANN, J., "À propos de la pepsine gastrique". Progrès Méd., 1922. 37:181.
43. MacLEAN, H., & GRIFFITHS, W.J., :-
 (a) "The factors influencing the concentration of Hydrochloric Acid during Gastric Digestion". Journ. Physiol.1928, 65:63-76.
 " " " " + WILLIAMS, B.W.
 (b) "Variations in the Acidity & Total Chloride contained in the Secretion from an Isolated Pavlov-Pouch in the dog". Ibid. pp.77-82.
44. MacLEAN, H., & GRIFFITHS, W.J., "The Automatic Regulation of Gastric Acidity". Journ.Physiol., 1928, 66: 356-70.

45. MacLEAN, H., "Modern views on digestion and gastric disease. Lond. 1926.
46. MANASSE, F., Pepsinwerte im fraktioniert ausgeheberten Magensaft. Münch. Med. Woch. 1926. 73: 1792-93.
47. MERING, J., Ueber die Function des Magens. Verhandl.Kon.Inn.Med. 1893, 12:471-482. (Quoted by MacLEAN (44))
48. METT, S.G., Beiträge zur Physiologie der Absonderungen. Arch.f.Anat.u.Physiol. 1894. Abthlg. 58-82.
49. MILLER, S., & SMITH, F.B., "Chlorides of Gastric Contents in relation to free acidity". Lancet, 1927. 1: 593-95.
50. OPFLER, B., "Zur Kenntniss vom Verhalten des Pepsins bei Erkrankungen des Magens." Centralblatt f.inn.Med. 1896. xvii.121-23.
51. OSLER, W., "William Beaumont. A pioneer American Physiologist." Journ.Amer.Med.Ass. 1902. 39:1223-32.
52. PATTERSON, J., "Fractional Test-Meal Analysis; simplified Technique with special reference to Chloride Estimations". Lancet, 1928, i, March, 24.
53. PAVLOV, I.P., "The Work of the Digestive Glands"; transl.W.H.Thompson, 2nd ed. London, 1910.
54. PFAÜNDLER, M., "Ueber eine neue Methode zur klinischen Funktionsprüfung des Magens und deren physiologische Ergebnisse. Deut.Archiv.f.Klin.Med., 1900. 65:255-84.
55. POULTON, E.P., "Gastric Secretion of Neutral Chloride". Brit.Med.Journ., 1928. 1:729-30.
56. PROUT, Wm. "On the nature of the acid and saline matters usually existing in the stomachs of animals." Phil. Trans.1824; pp. 45-49.

57. REAUMUR, M. de, "Sur la Digestion des Oiseaux"
Mem.Acad.Sci. Paris 1752. 66: 266.
58. REHFUSS, M.E., "Diseases of the Stomach".
(W.B.Saunders) Phila., 1927.
59. RIZANTZEFF, N.V., "Sur le suc gastrique du
chat", Archiv. des Sci.Biol. St.Pet-
ersburg, 1895. 3: 216-225. [Quoted by
BOLDIREV (7).]
60. ROBERTS, M., "The Fasting Gastric Secretion in
Man". Quart. Journ. Med., 1927-28.
XXI. 7-19.
61. RONA, P., & KLEINMANN, H., "Nephelometrische
Untersuchungen über fermentative Ei-
weisspaltung". Biochem. Zeitschr., 1924
150: 444-67.
62. ROSEMANN, R., "Beiträge zur Physiologie der
Verdauung:- 1. Die Eigenschaften und
die Zusammensetzung des durch Schein-
fütterung gewonnenen Hundemagensaftes".
Pflug.Archiv. 1907. 118: 467-524.
63. ROSEMANN, R., "Zur Physiologie und Pathologie
der Säureabsonderung der Magenschleim-
haut". Virch.Archiv., 1920. 229: 67-
89.
64. ROSTOCK, P., "Pepsinbestimmung im Magensaft",
Münch. Med. Woch., 1924. 71: 1311-12.
65. ROTH, W., & STRAUSS, H., "Untersuchungen über
den Mechanismus der Resorption und
Sekretion im menschlichen Magen".
Zeit.f.Klin.Med., 1899. 37: 144-93.
[Quoted by MacLEAN (44)]
66. ROTHSCHILD, F.,
Archiv. f. Verdauungskr., 1928. 42: 57.
No. 73.
67. SCHÜTZ, E., "Eine Methode zur Bestimmung der
relativen Pepsinmenge". Zeitschr. f.
Physiol.Chem., 1885. 9: 577-90.
68. SCHÜTZ, J., "Zur Kenntniss der quantitativen
Pepsinwirkung". Zeitschr. f. physiol.
Chem., 1900. 30: 1-14.

69. SCHWANN, TH., "Ueber das Wesen des Verdauungsprocesses". Archiv. f. Anat. und Physiol., 1836, Physiol.Abthg. 20: 138
 70. SMITH, R. MEADE, "Die Resorption des Zuckers und des Eiweisses im Magen". Archiv. f. Anat. und Physiol., 1884. Physiol. Abth. p.481-96. [Quoted by MacLEAN (44)].
 71. SPALLANZANI, L., (l'Abbé) "Expériences sur la digestion de l'homme et de différentes espèces d'animaux". Lausanne, 1785.
 72. SPENCER, W.H., MEYER, G.P., REHFUSS, M.E., & HAWK, P.P., "Direct Evidence of Duodenal Regurgitation and its Influence upon the Chemistry & Function of the Normal Human Stomach". Am. Journ. Physiol. 1916 39:459-479.
 73. STEINITZ, H., "Der Chlorabscheidung des menschlichen Magens in ihren Beziehungen zu pathologischen Vorgängen". Archiv. f. Verdauungskr., 1928. 42: 57-104.
 74. WAKSMAN, S.A., & DAVISON, W.C., "Enzymes" London (Baillière, Tindall & Cox), 1926.
 75. WASMANN, A., "Oe digestionem nonnulla". Diss. Berlin, 1839. [Quoted by E.A.SCHAFER, "Textbook of Physiology", 1898]
-

ONE HUNDRED CHARTS

REPRESENTING VARIETIES of CHLORIDES and ACID.
VARIATIONS

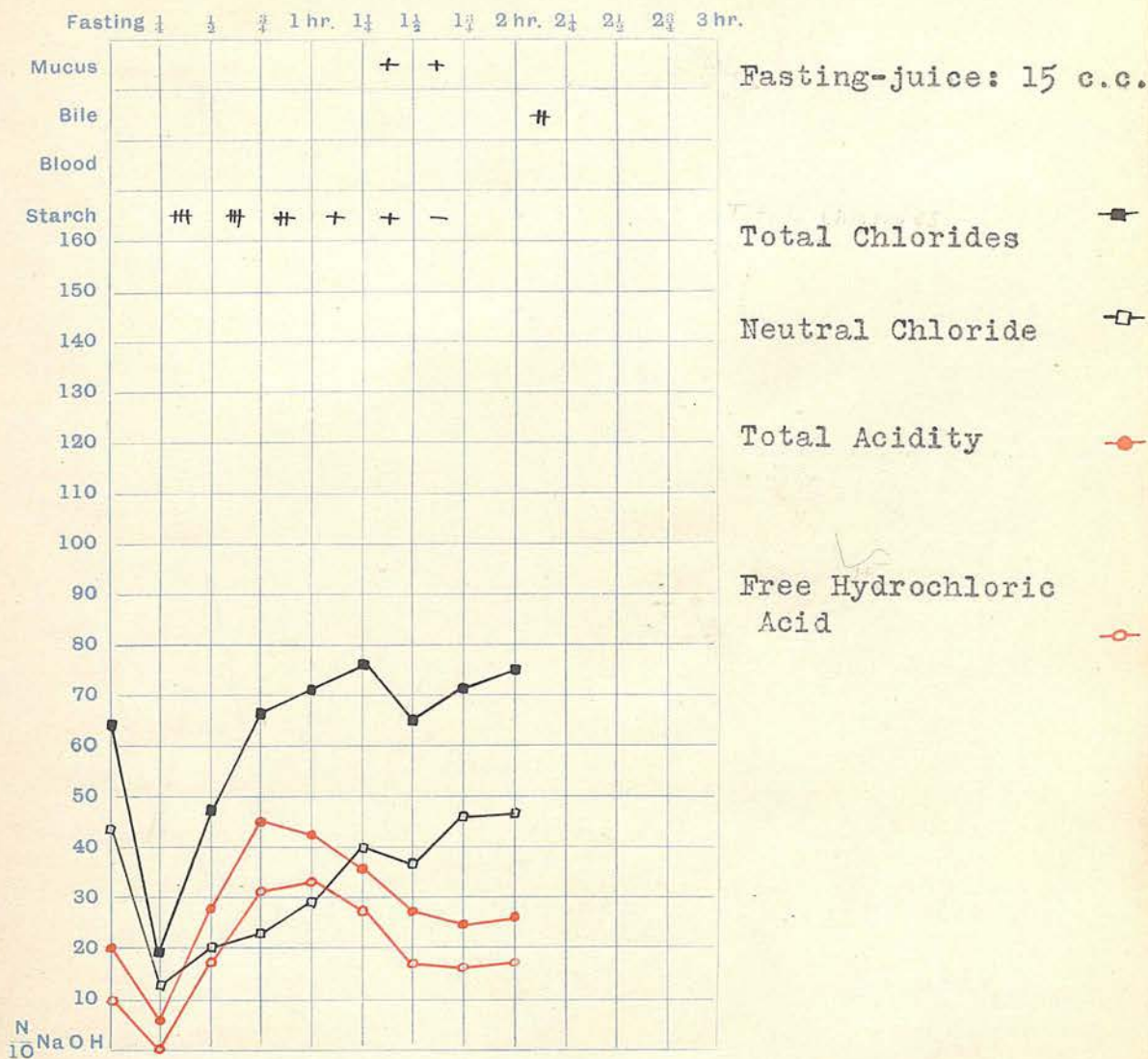
Name of Patient

// N 1.

(M. aet. 35)

1. FRACTIONAL TEST-MEAL.

Date 21 6. '29.

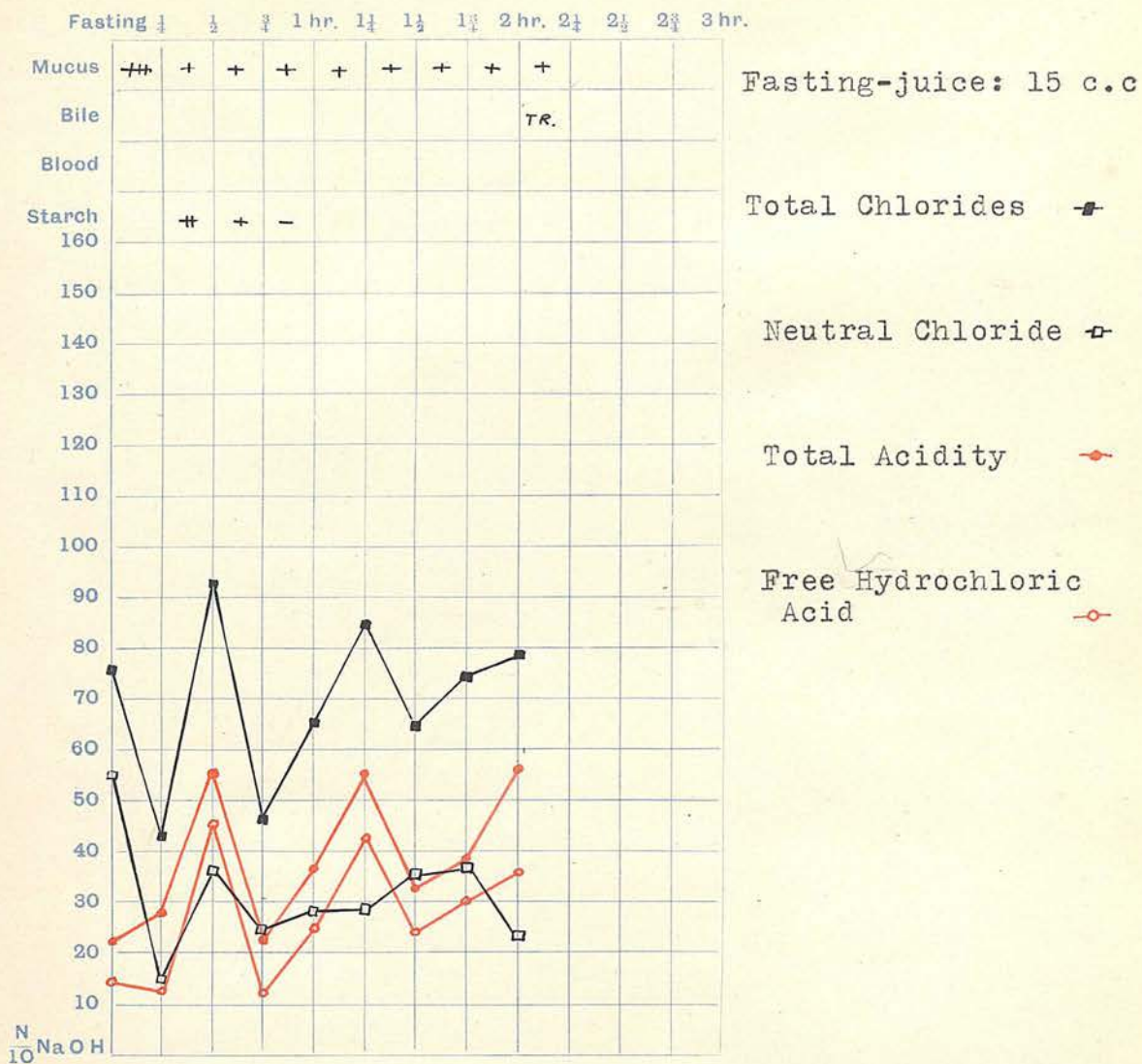


Normal Subject.

Name of Patient N 2. (M. aet. 32)

1. FRACTIONAL TEST-MEAL.

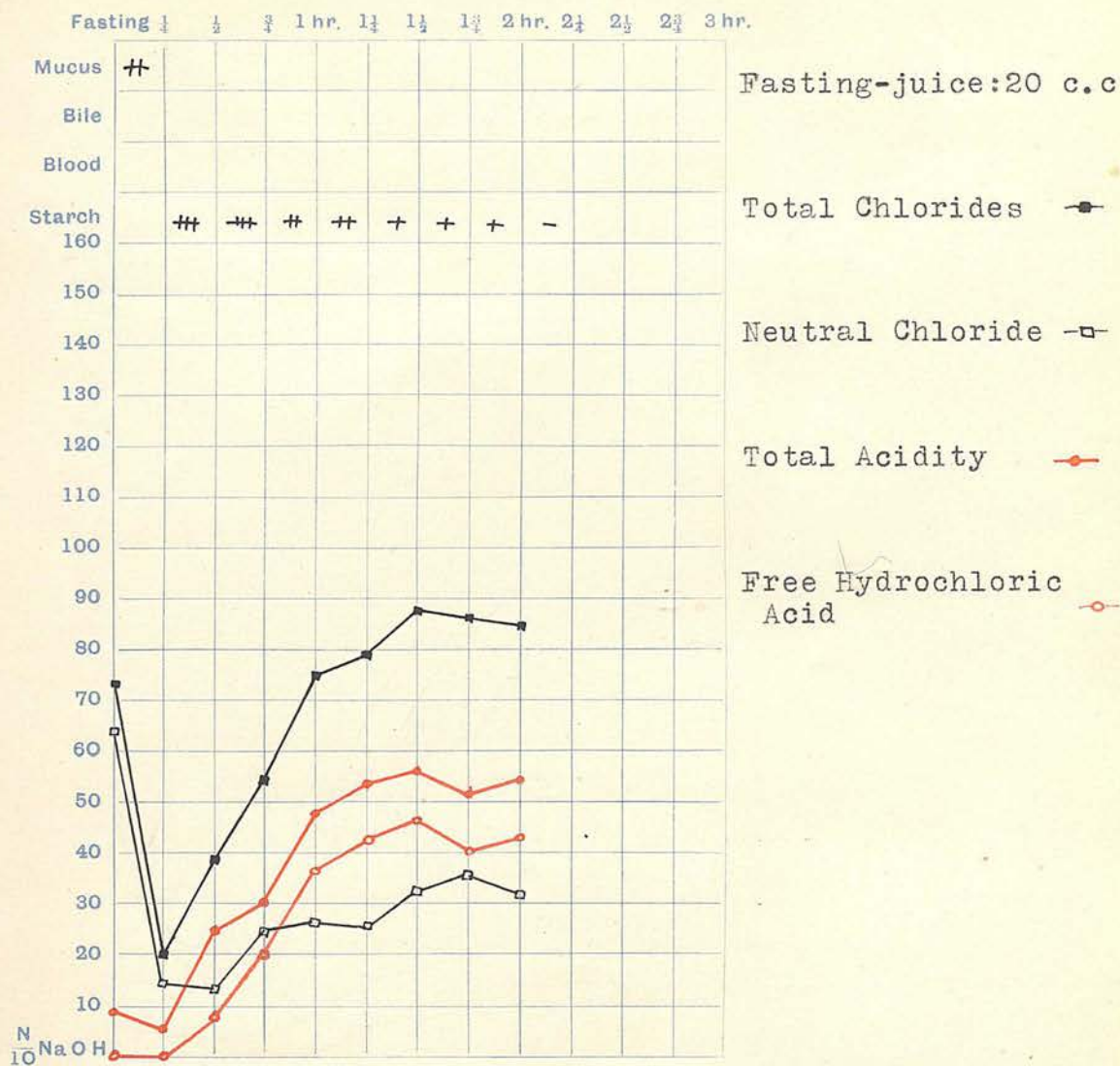
Date 8. 7. '29.



Normal Subject

Name of Patient N 3. (M. aet. 28)

1. FRACTIONAL TEST-MEAL. Date 16. 7. '29.



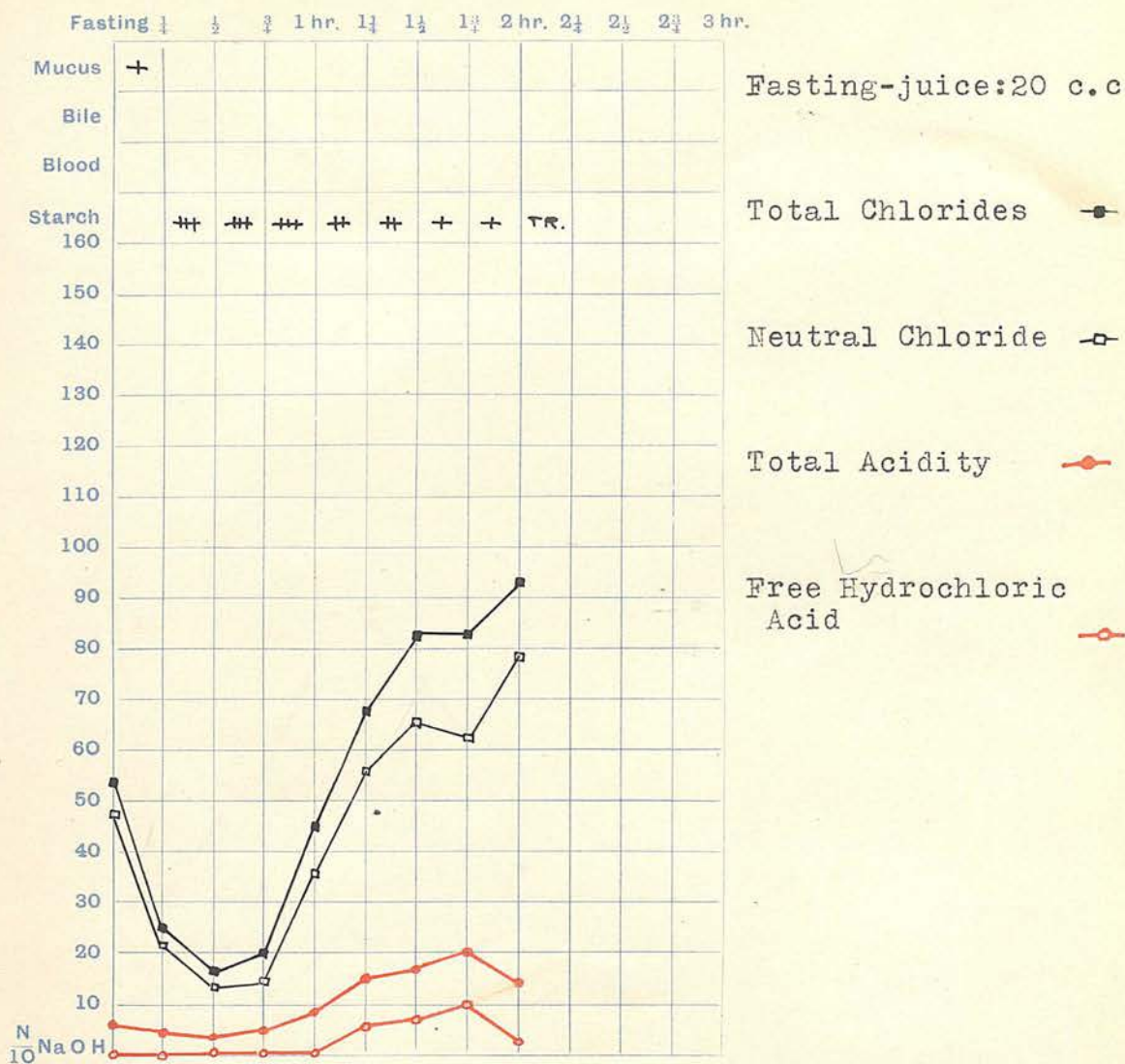
Normal Subject

Name of Patient N 4

(M. aet. 26)

1. FRACTIONAL TEST-MEAL.

Date 16. 7. '29.



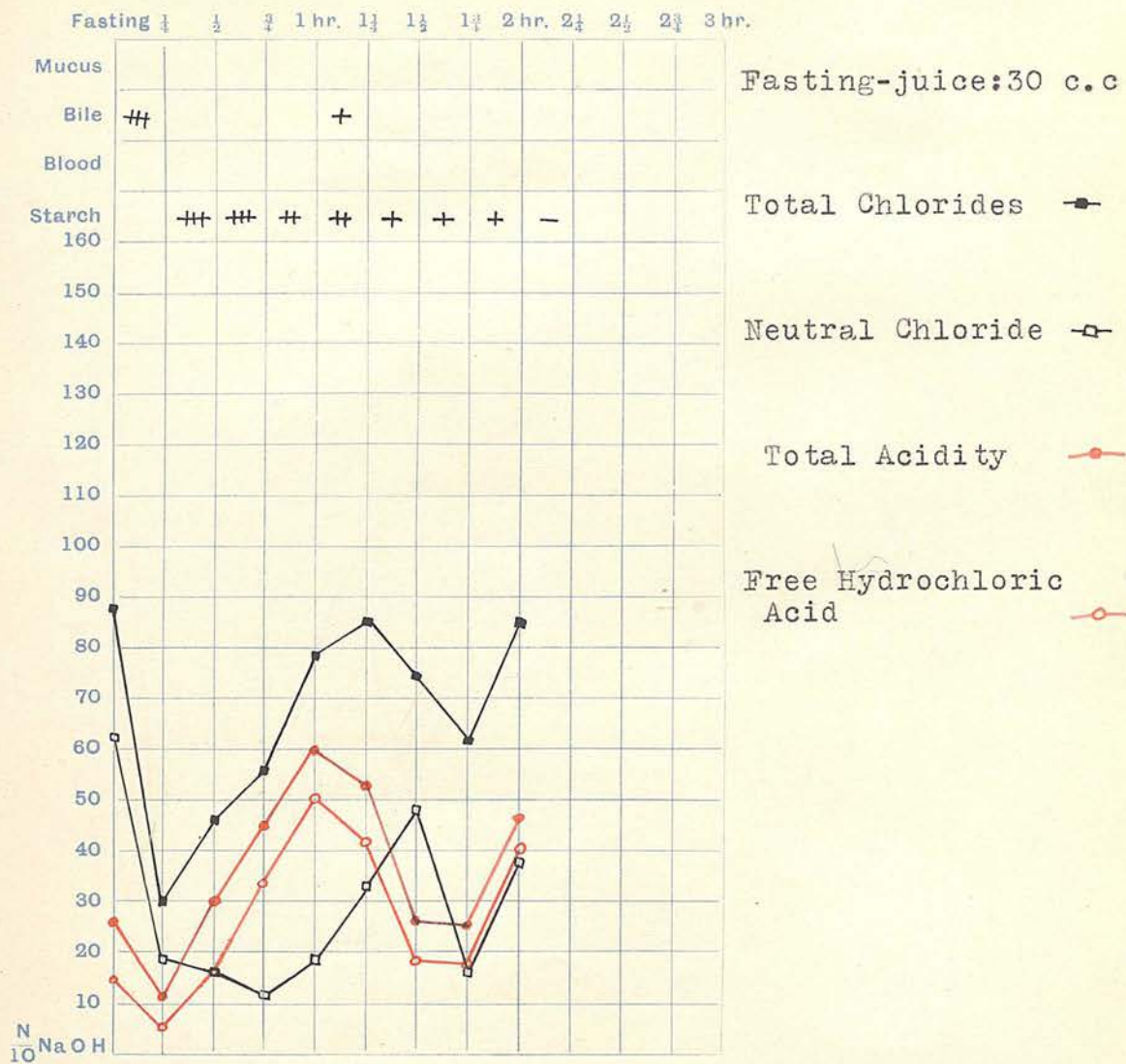
Normal Subject

Name of Patient N 5.

(M. 27)

1. FRACTIONAL TEST-MEAL.

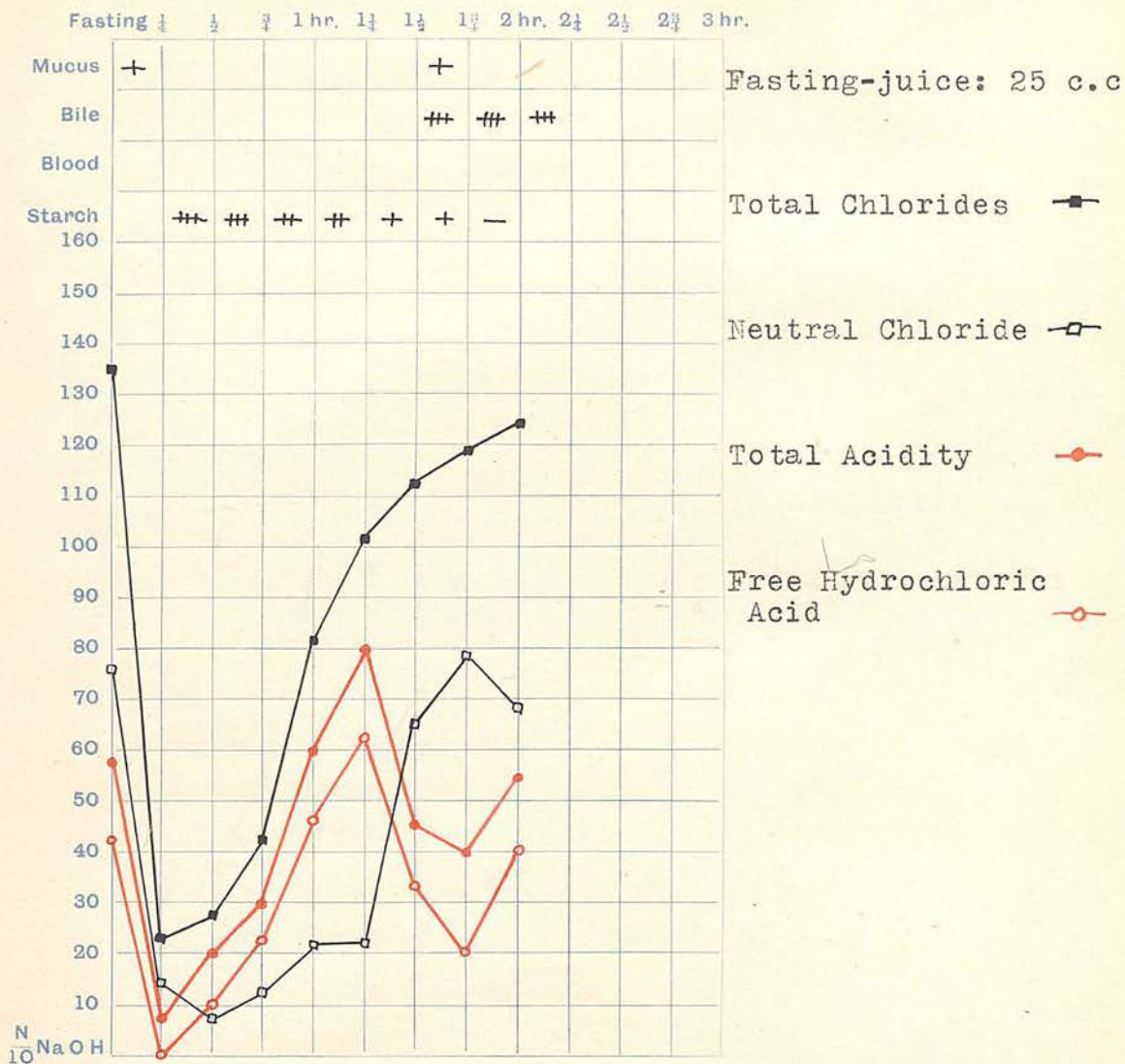
Date 16. 7. '29.



Normal Subject

Name of Patient N 6. (F. aet. 54)

1. FRACTIONAL TEST-MEAL. Date 14. 3. '29.

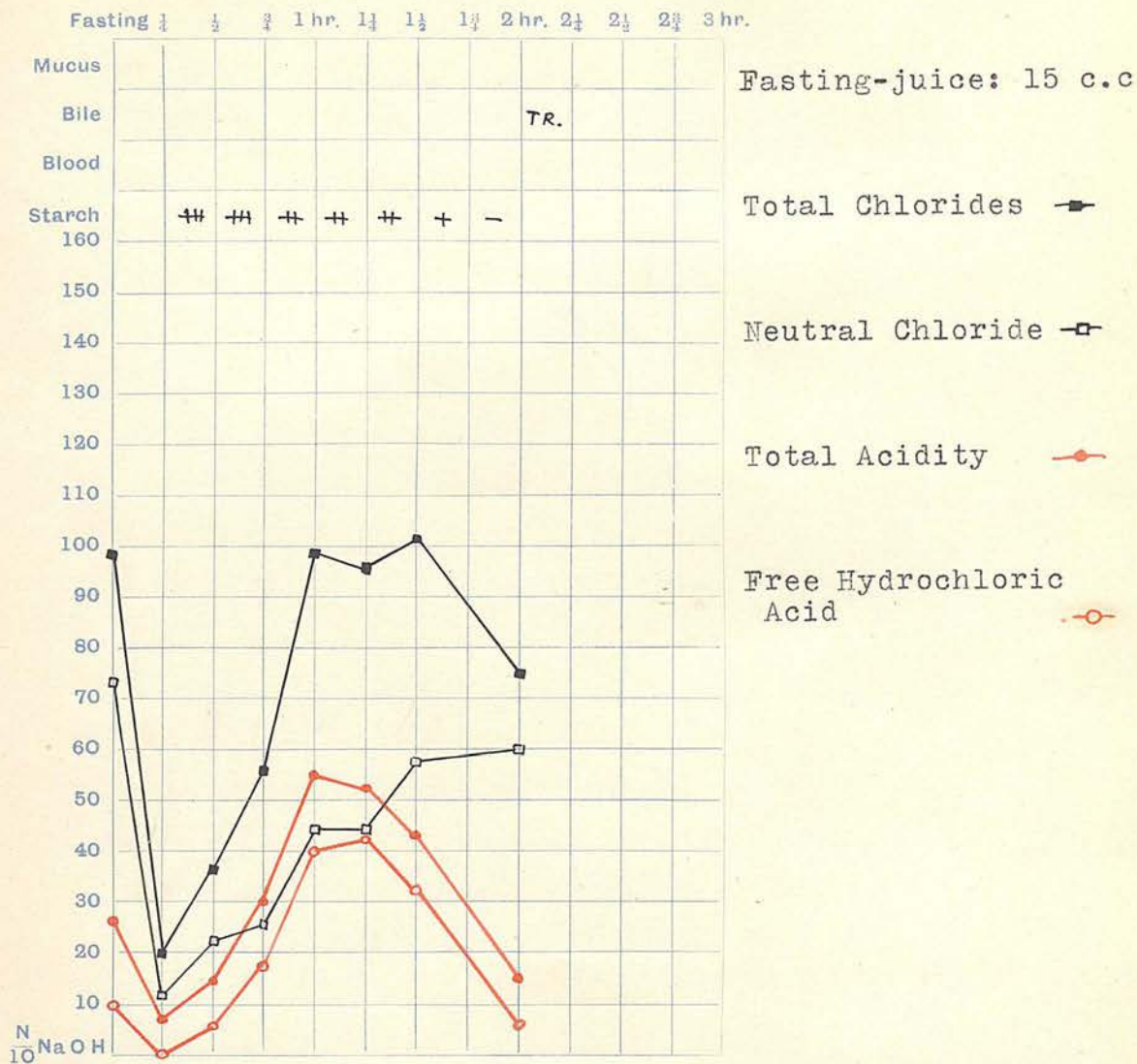


Normal Subject

Name of Patient N 7. (M. aet. 49)

1. FRACTIONAL TEST-MEAL.

Date 8. 7. '29.

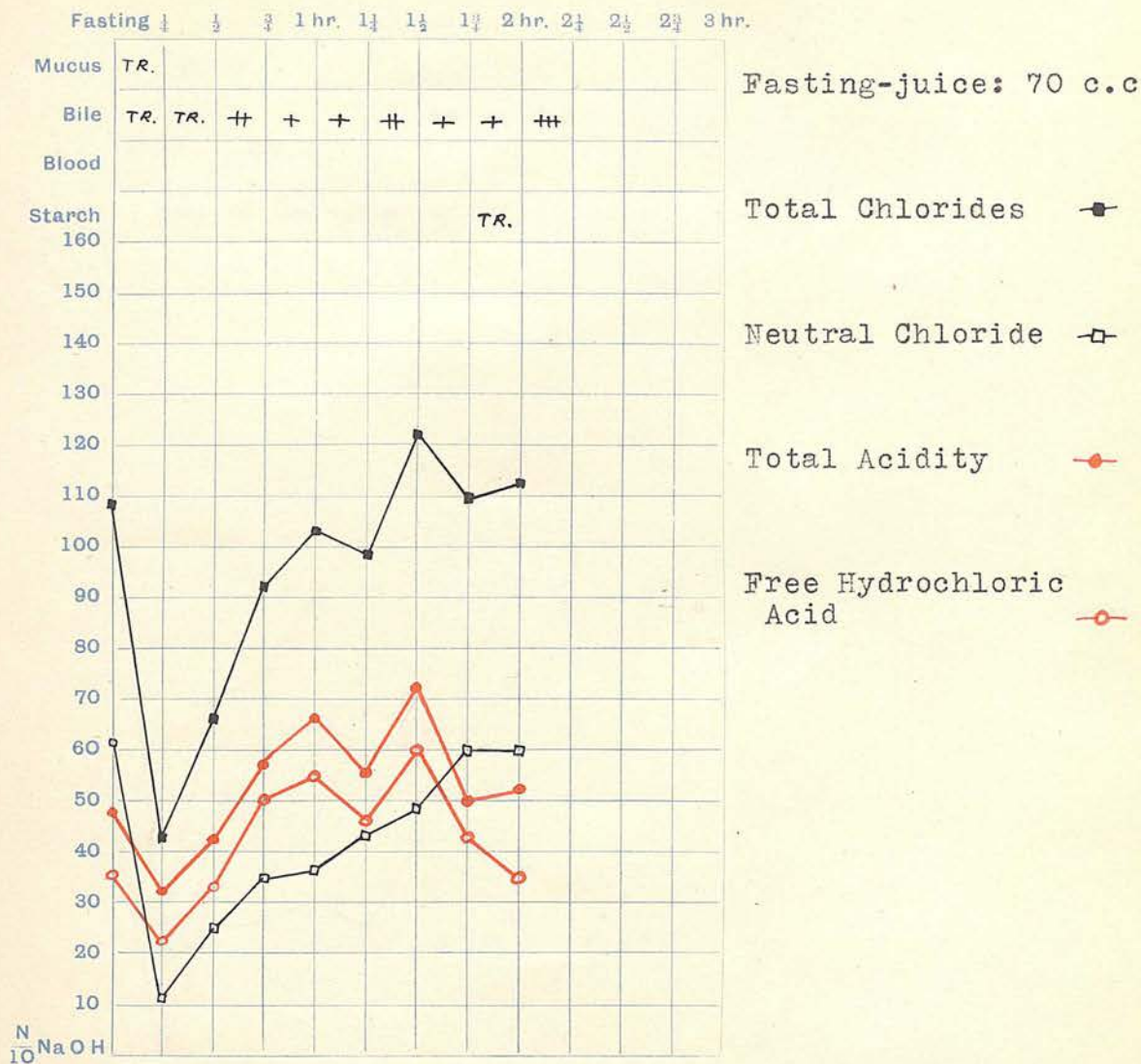


Normal Subject

Name of Patient N 8. (M. aet. 30)

1. FRACTIONAL TEST-MEAL.

Date 9. 7. '29.



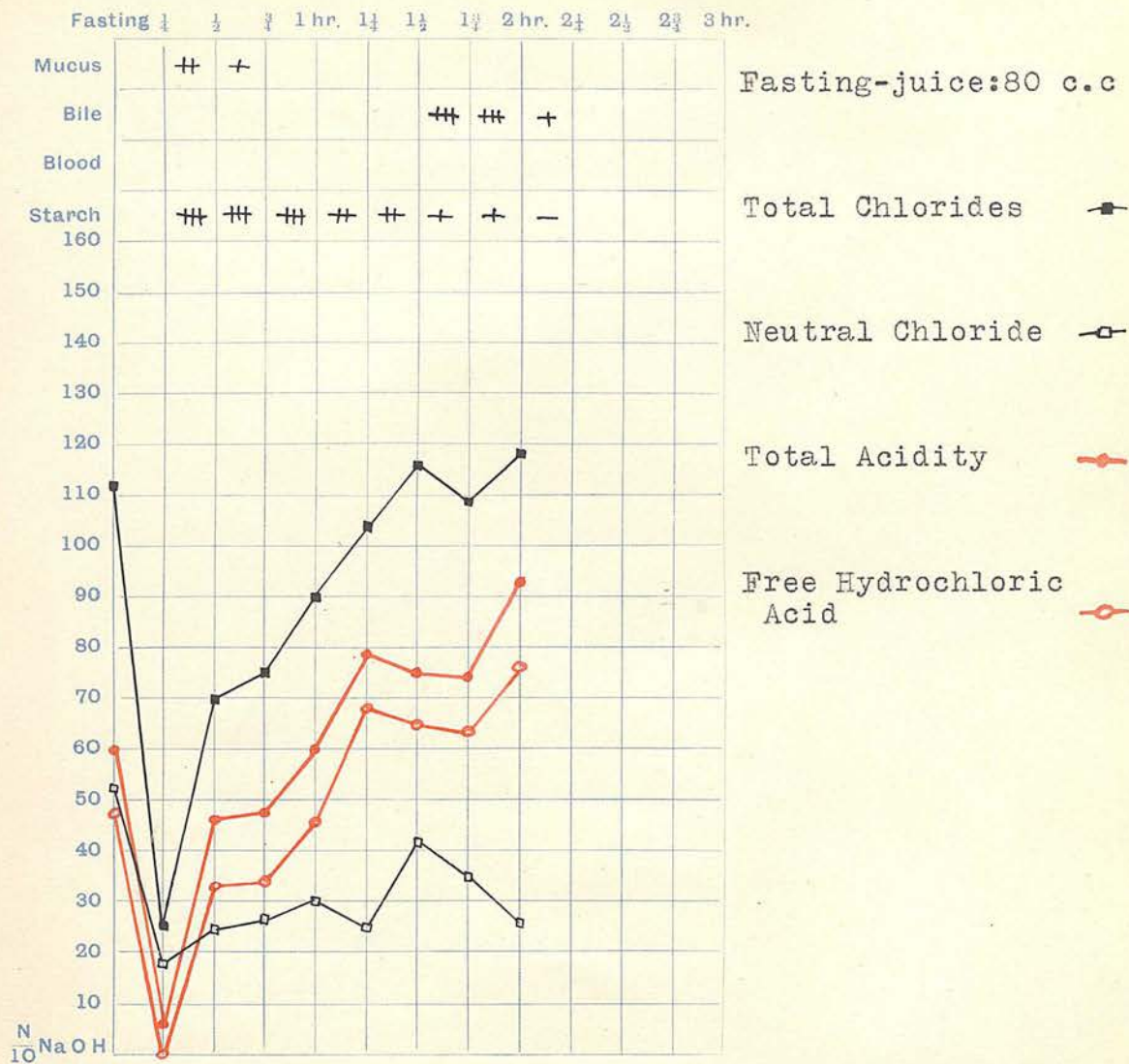
Normal Subject

Name of Patient N 9.

(M. aet. 24)

1. FRACTIONAL TEST-MEAL.

Date 13. 7. '29.



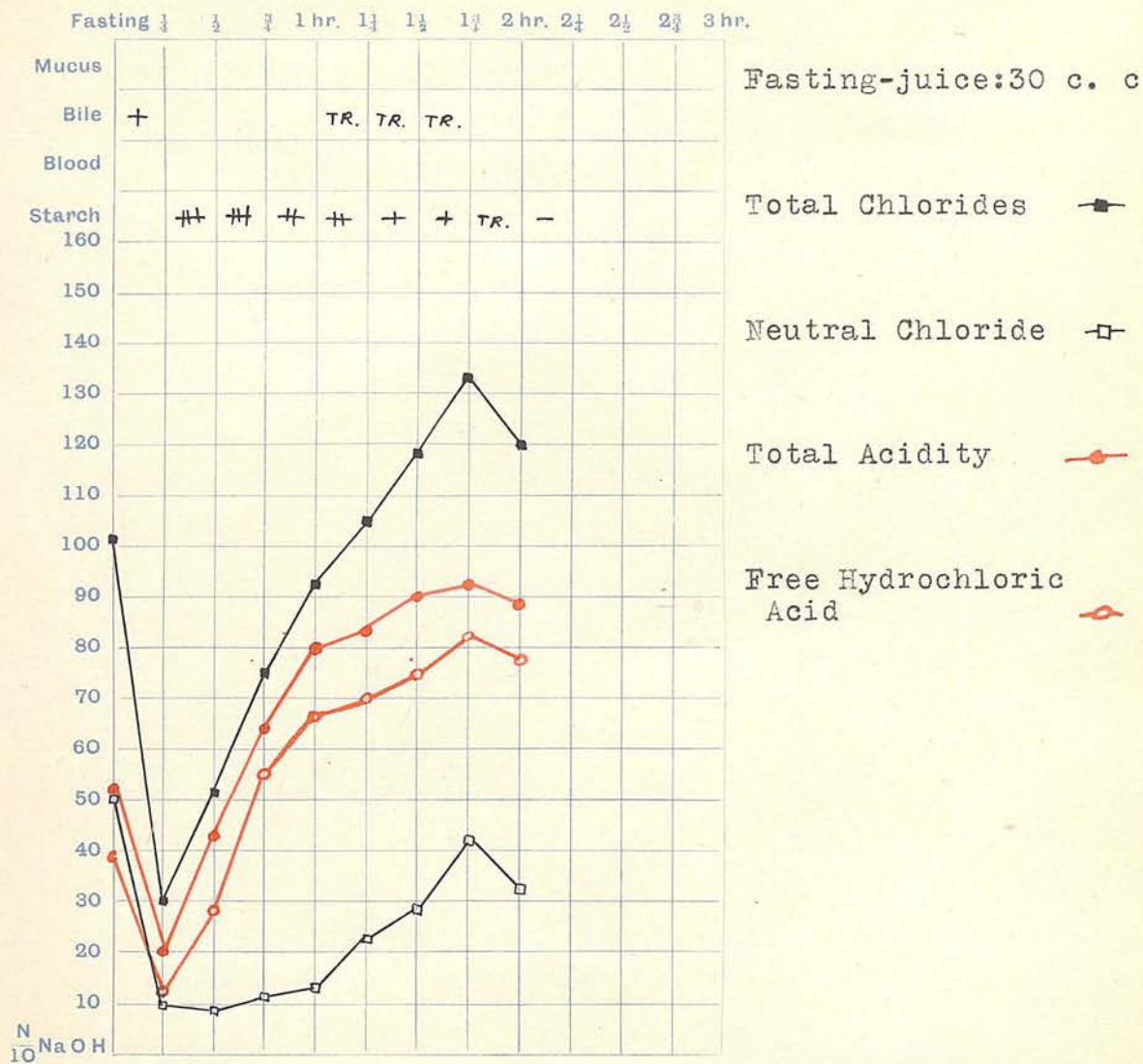
Normal Subject

Name of Patient N 10.

(M. aet. 26)

1. FRACTIONAL TEST-MEAL.

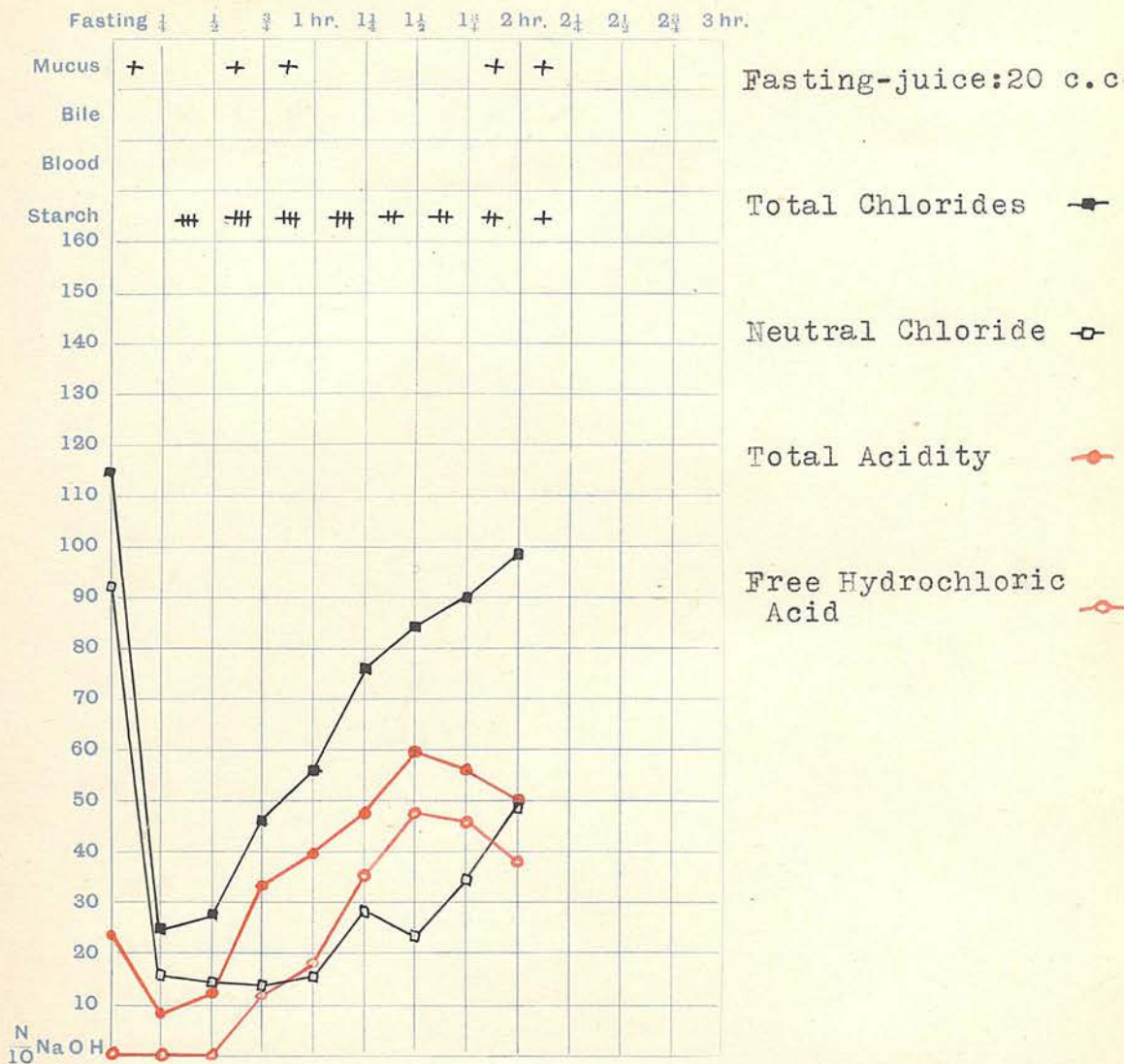
Date 13. 7. '29.



Normal Subject

Name of Patient UV 1.(A) (F. aet. 48)

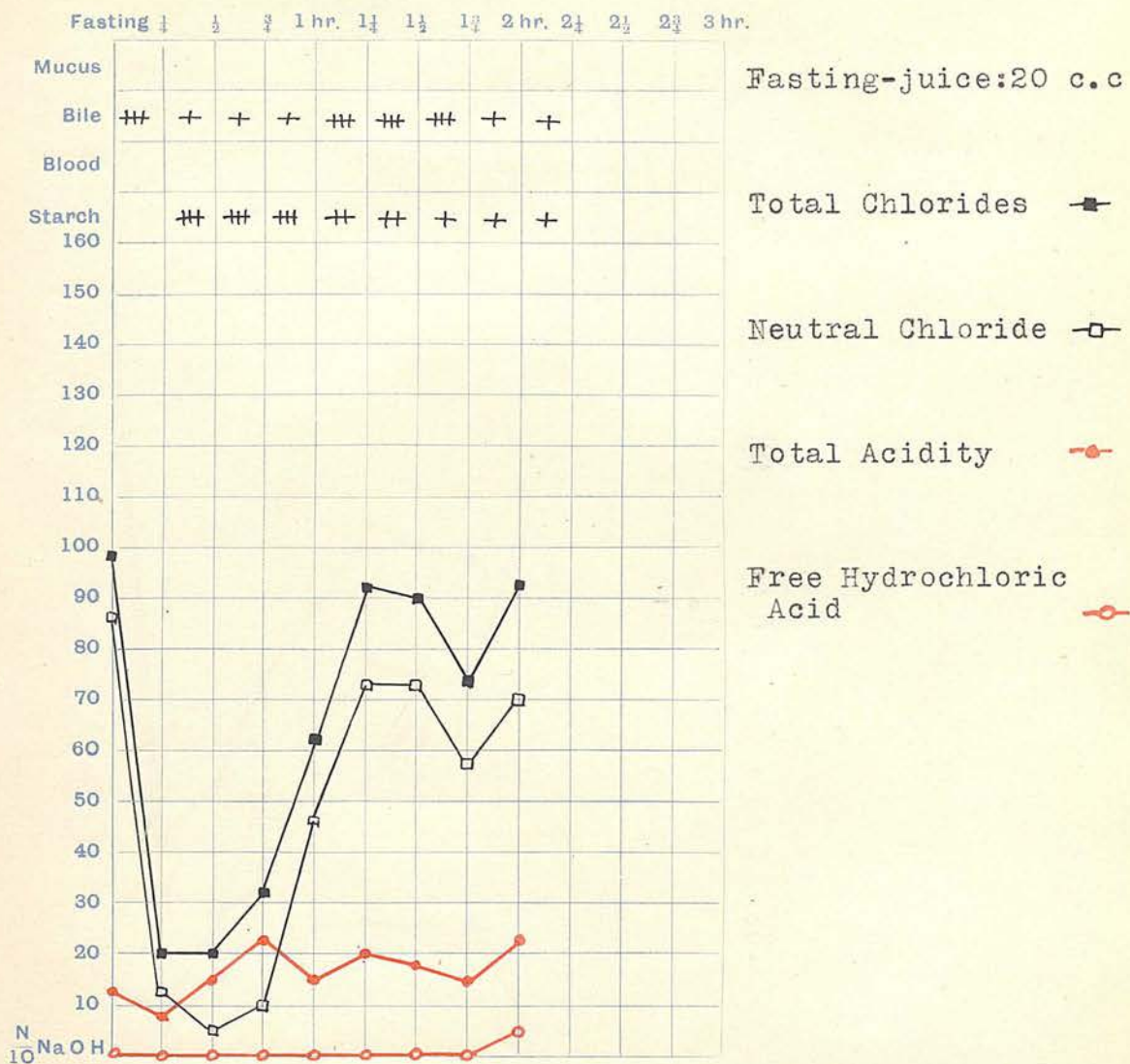
1. FRACTIONAL TEST-MEAL. Date 6. 3. '29.



Gastric ulcer lesser curvature, preoperative.

Name of Patient UV 1.(B) (F. aet. 48)

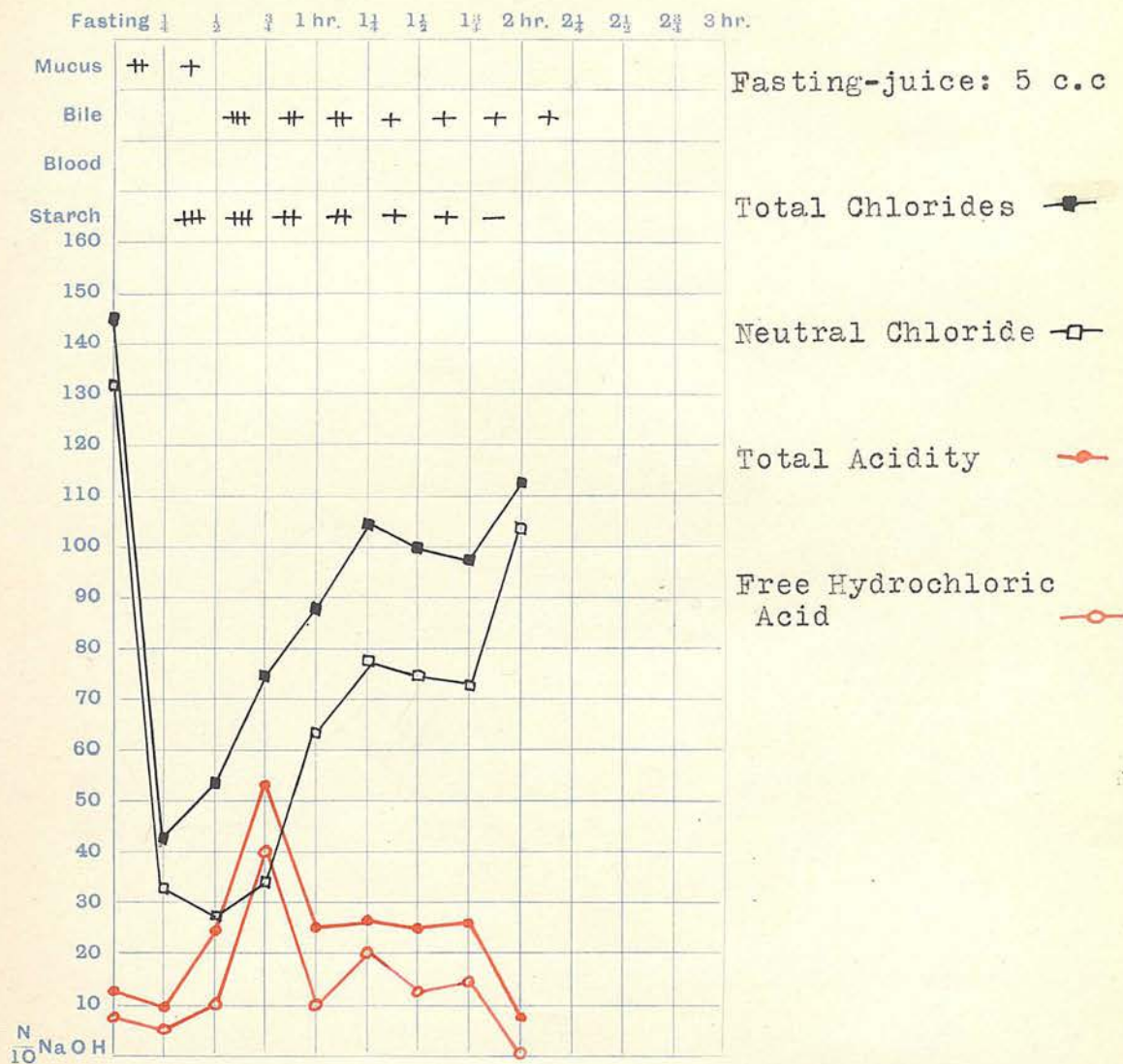
1. FRACTIONAL TEST-MEAL. Date 27. 3. '29.



Three weeks after gastroenterostomy.

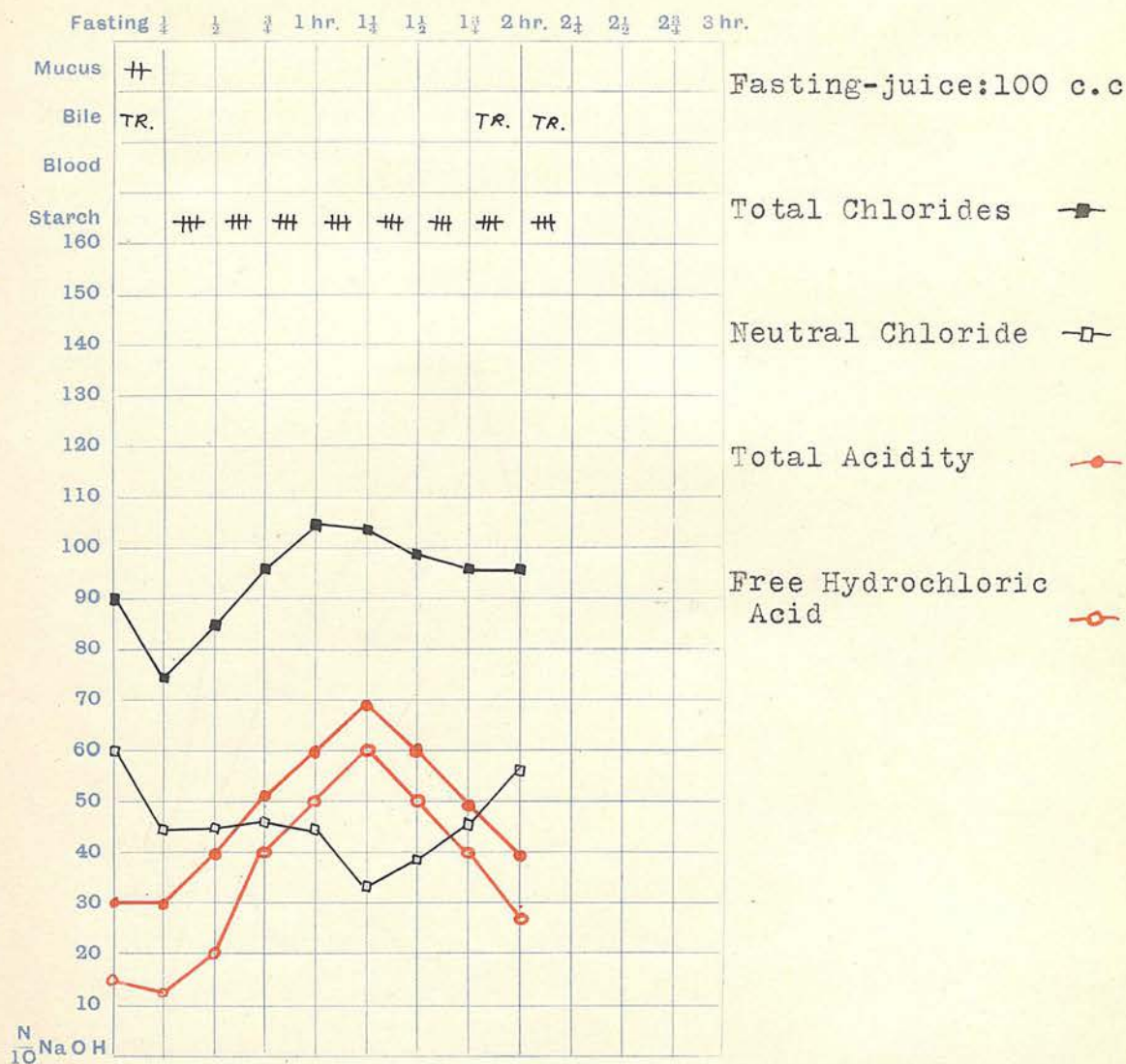
Name of Patient UV 1.(C) (F. aet. 48)

1. FRACTIONAL TEST-MEAL. Date 29. 5. '29.



Three months after gastroenterostomy.

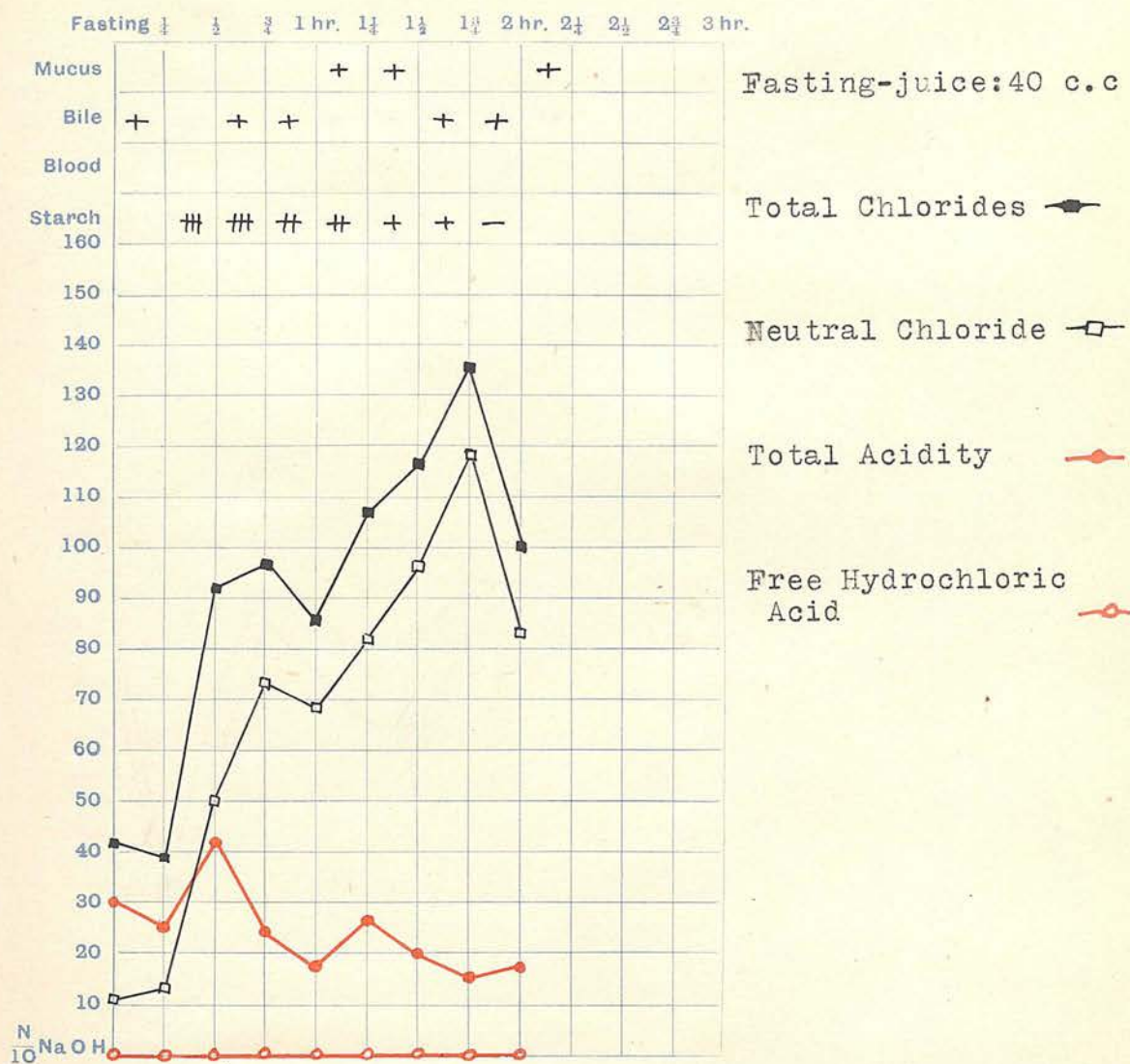
1. FRACTIONAL TEST-MEAL Date 24. 5. '28.



Gastric ulcer, pyloric stenosis, preoperative.

Name of Patient UV 2.(B) (M. aet. 36)

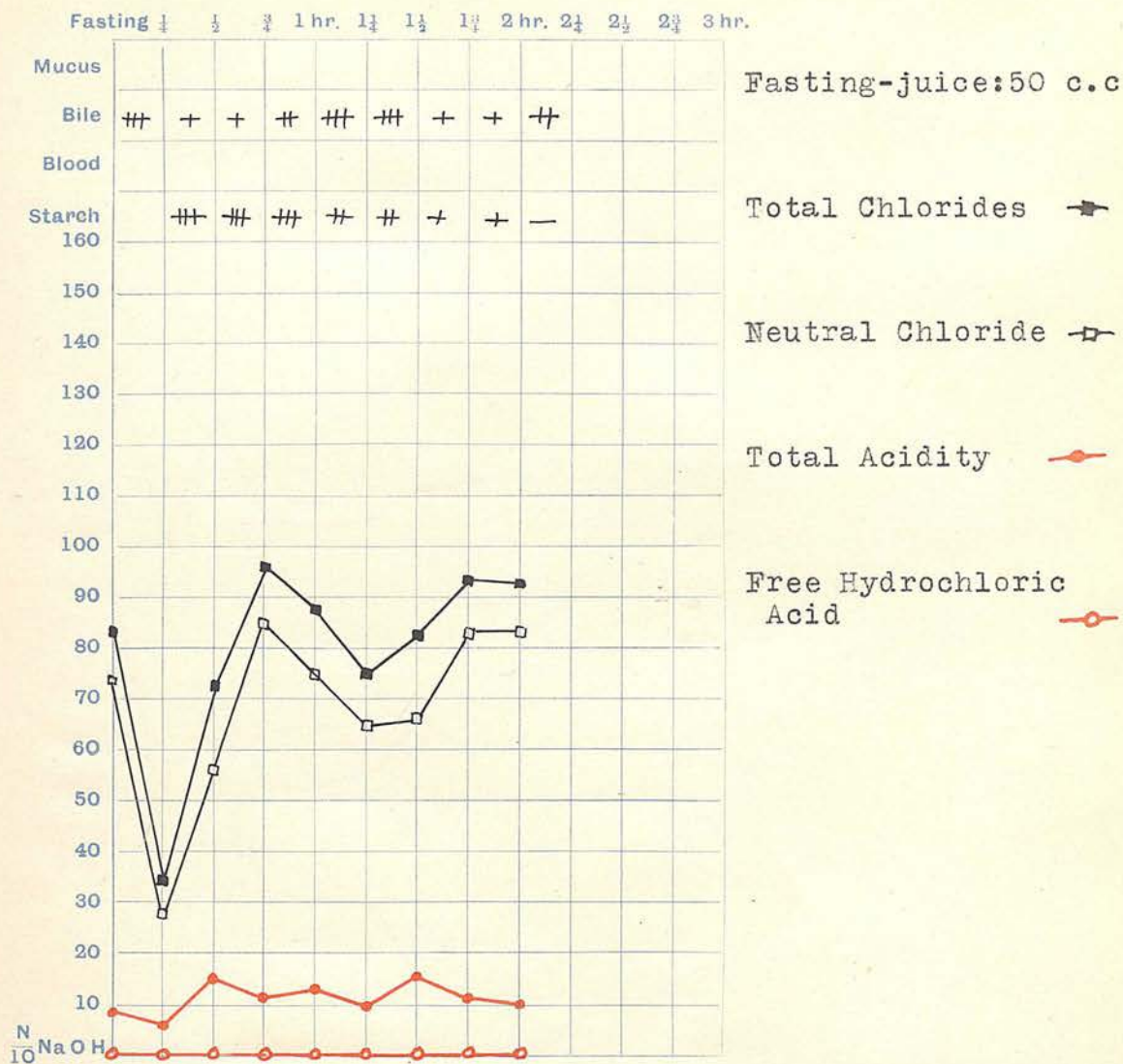
1. FRACTIONAL TEST-MEAL. Date 7. 6. '28.



Two weeks after gastroenterostomy.

Name of Patient UV 2.(C) (M. aet. 37)

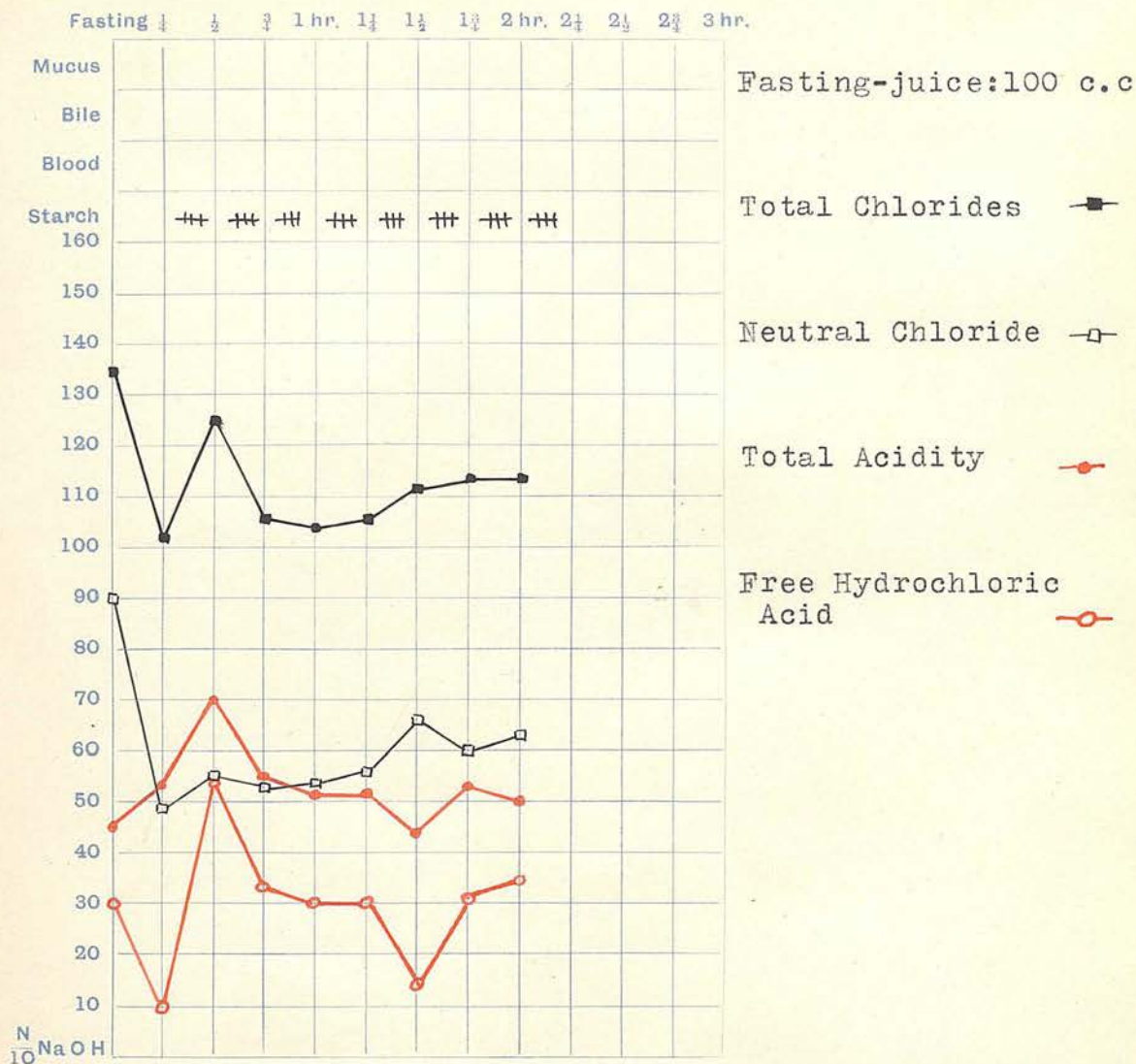
1. FRACTIONAL TEST-MEAL. Date 2. 6. '29



Twelve months after gastroenterostomy.

Name of Patient UV 3.(A) (M. aet. 39)

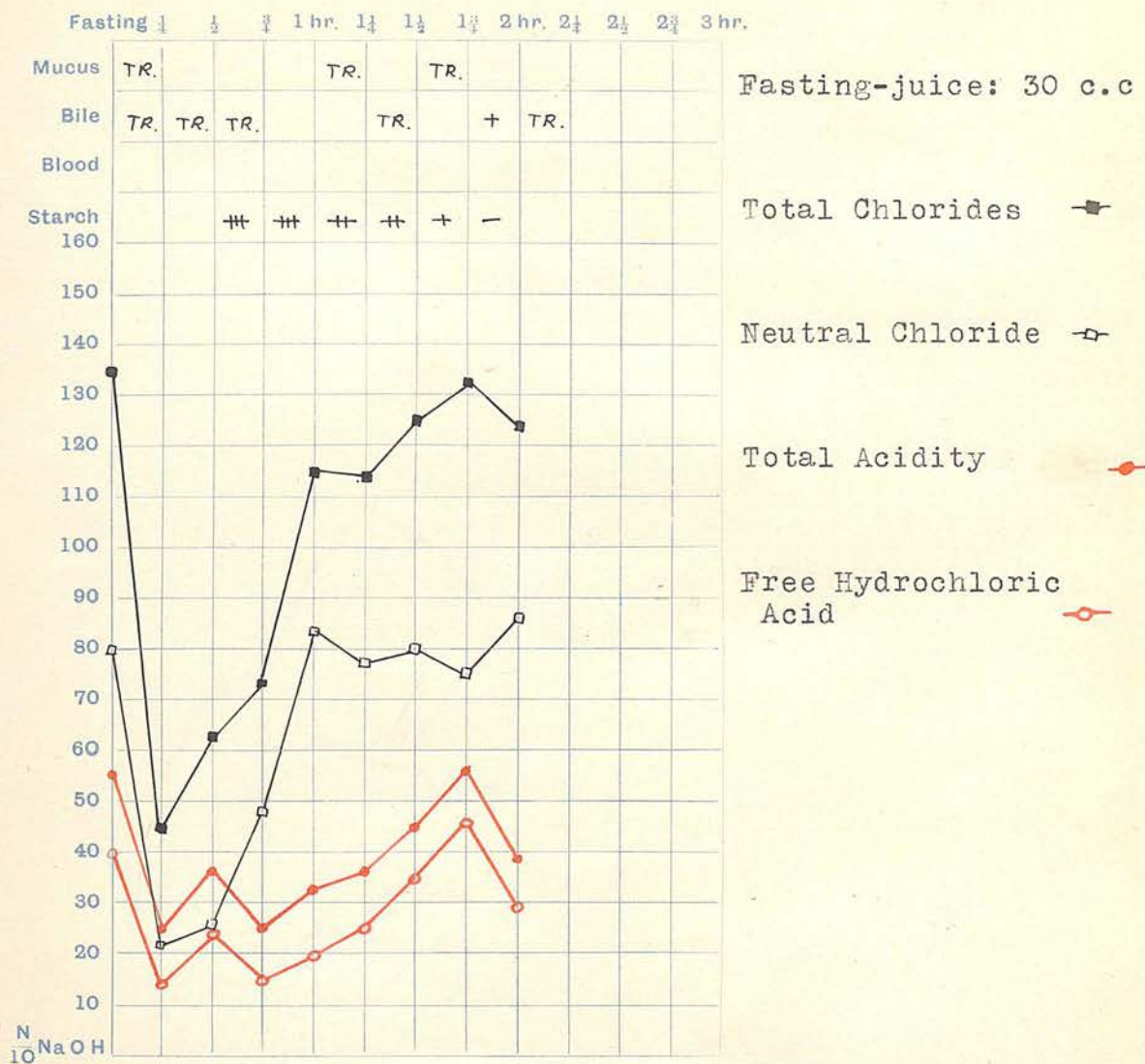
1. FRACTIONAL TEST-MEAL. Date 26. 5. '28.



Gastric ulcer, pyloric stenosis, preoperative.

Name of Patient UV 3.(B) (M. aet. 39)

1. FRACTIONAL TEST-MEAL. Date 22. 6. '28.



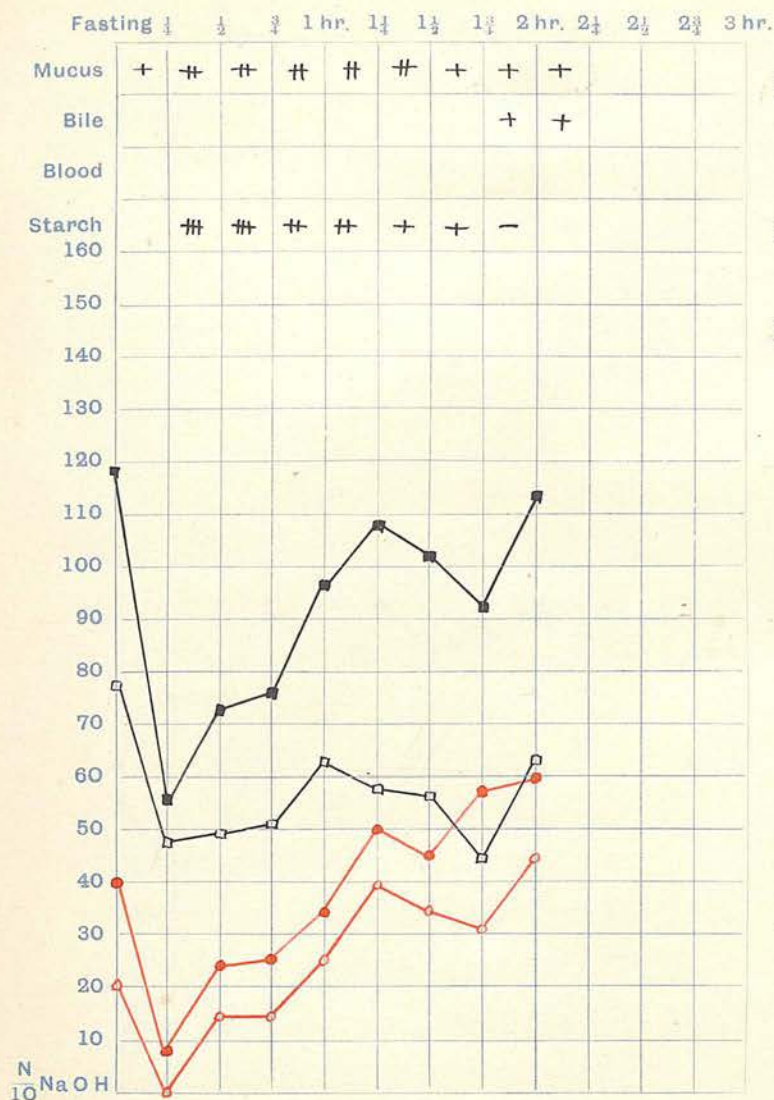
Four weeks after gastroenterostomy.

Name of Patient UV 4.

(M. aet. 52)

1. FRACTIONAL TEST-MEAL.

Date 27. 5. '28.



Fasting-juice: 40 c.c.

Total Chlorides

Neutral Chloride

Total Acidity

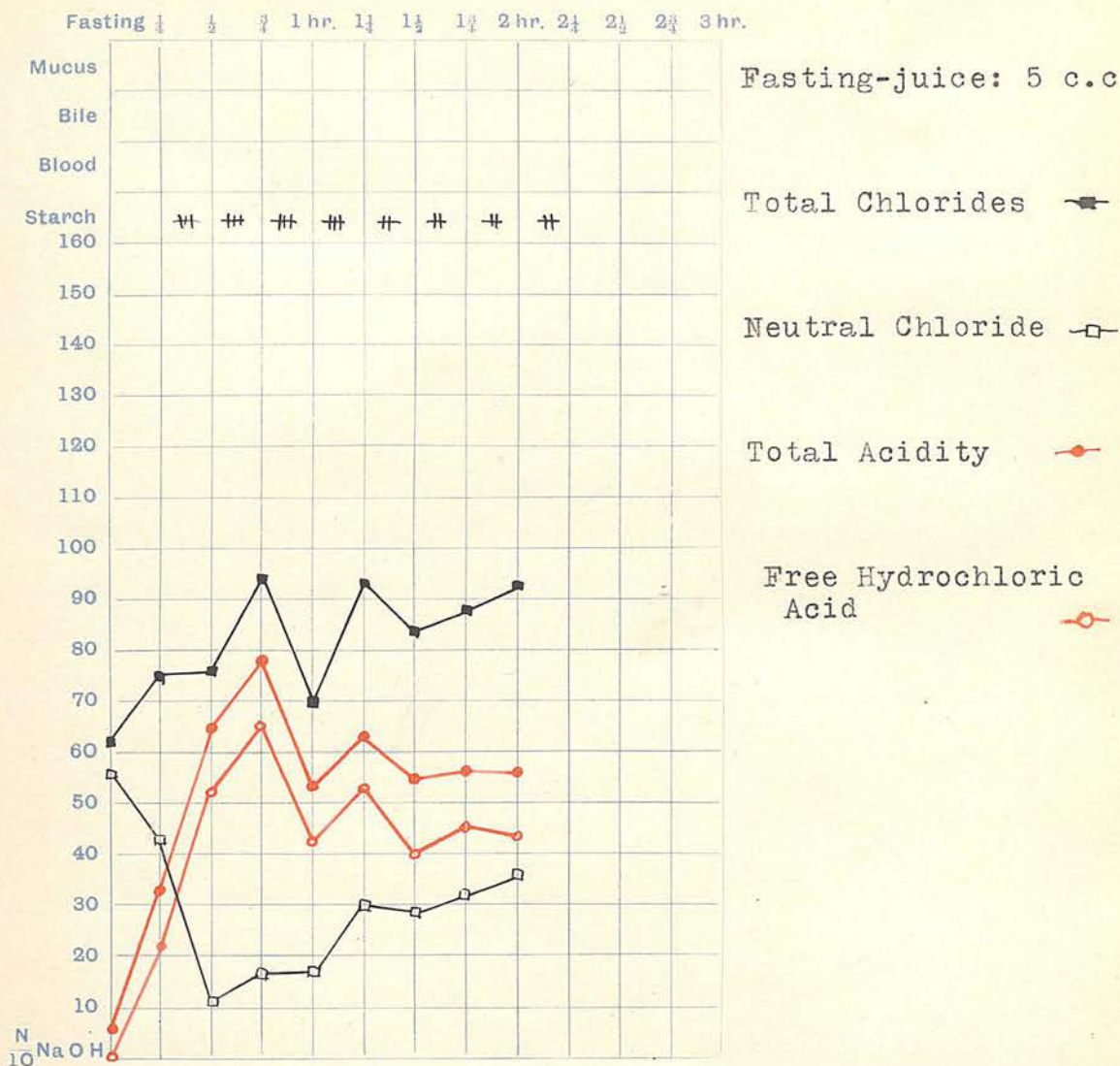
Free Hydrochloric Acid.

Gastric ulcer, lesser curvature.

Name of Patient UV 5. (F. aet. 50)

1. FRACTIONAL TEST-MEAL.

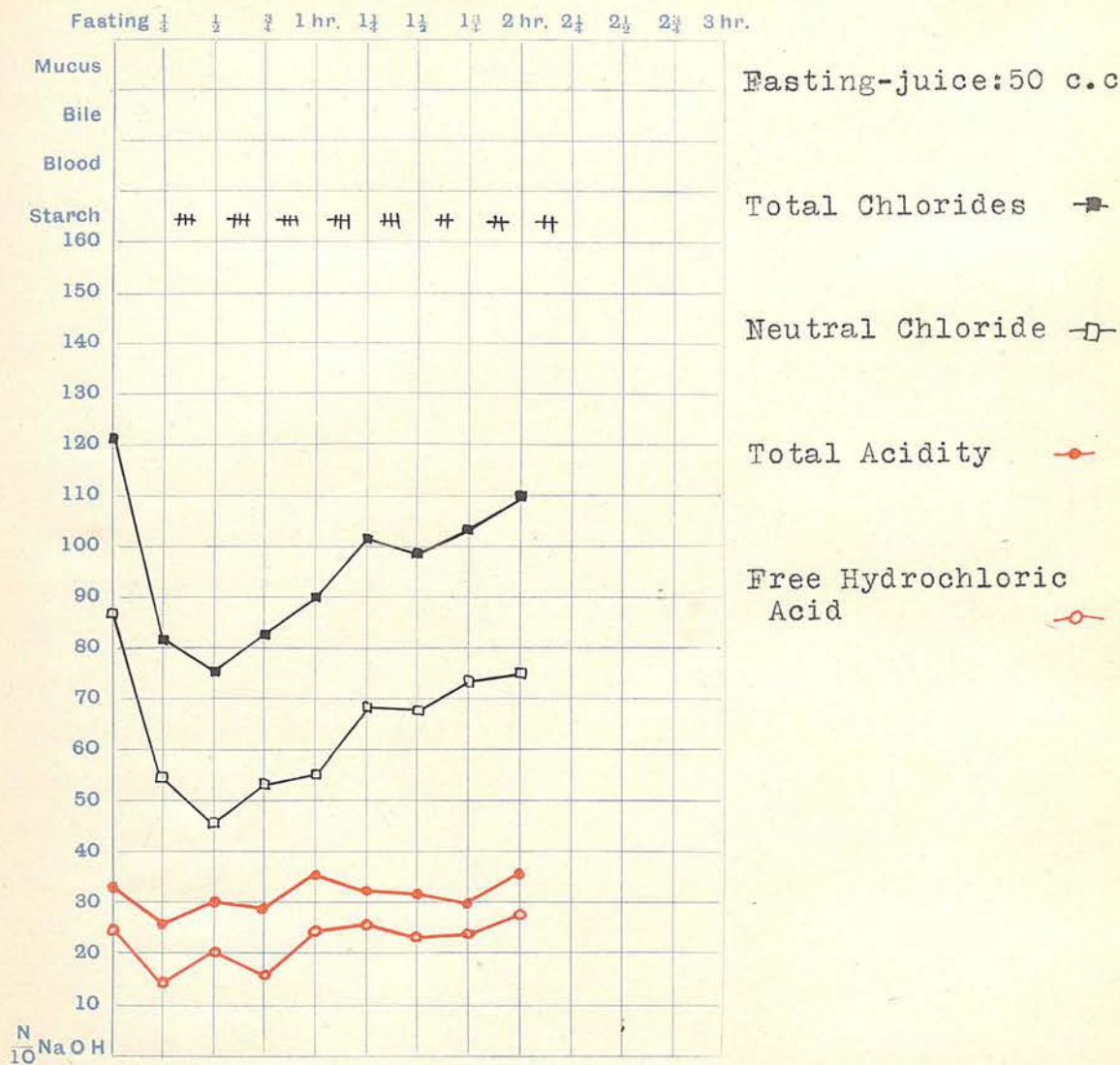
Date 2. 5. '29



Gastric ulcer, lesser curvature.

Name of Patient UV 6. (F. aet. 47)

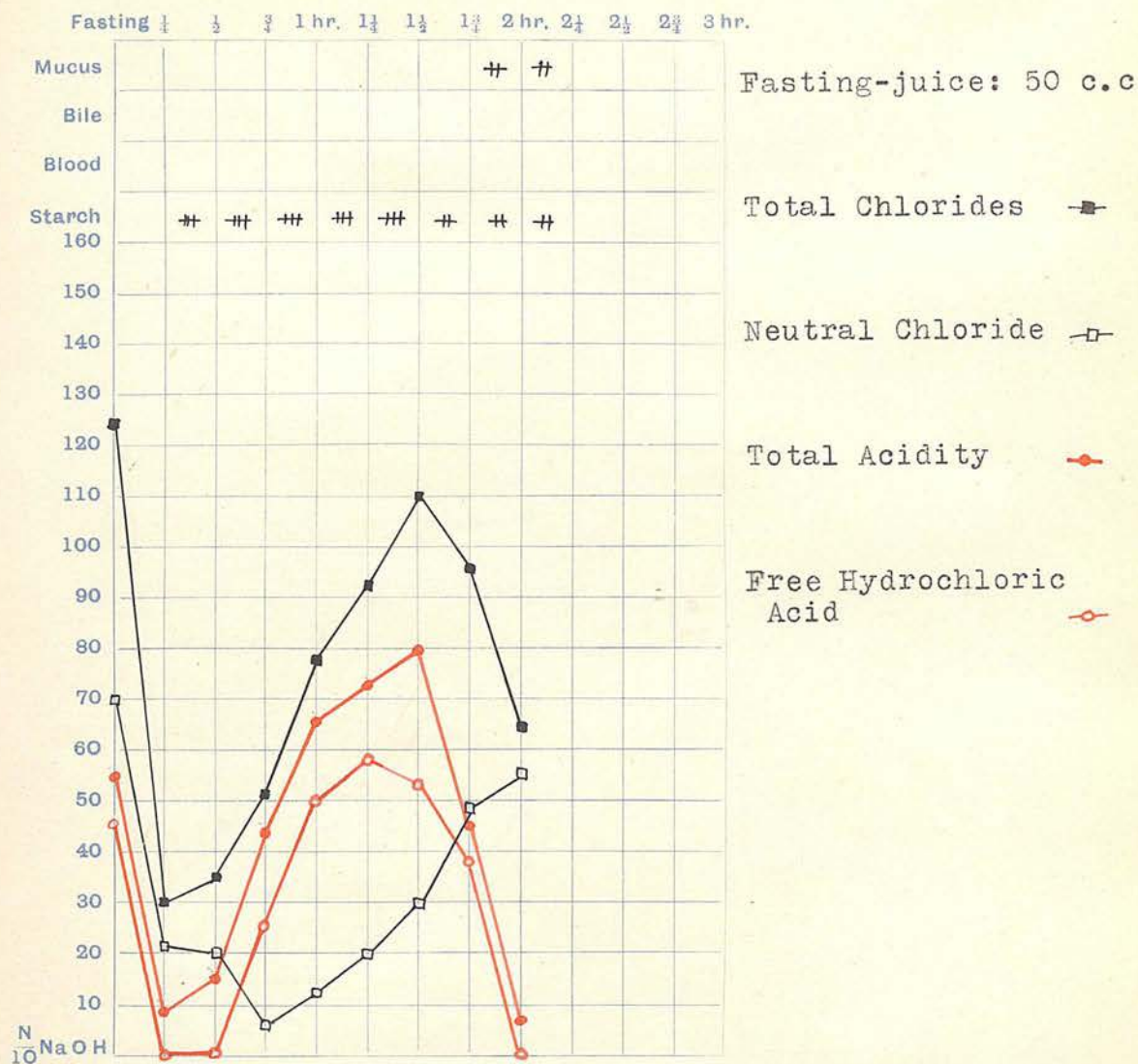
1. FRACTIONAL TEST-MEAL. Date 11. 2. '29.



Gastric ulcer, pyloric stenosis.

Name of Patient UV 7. (F. aet. 51)

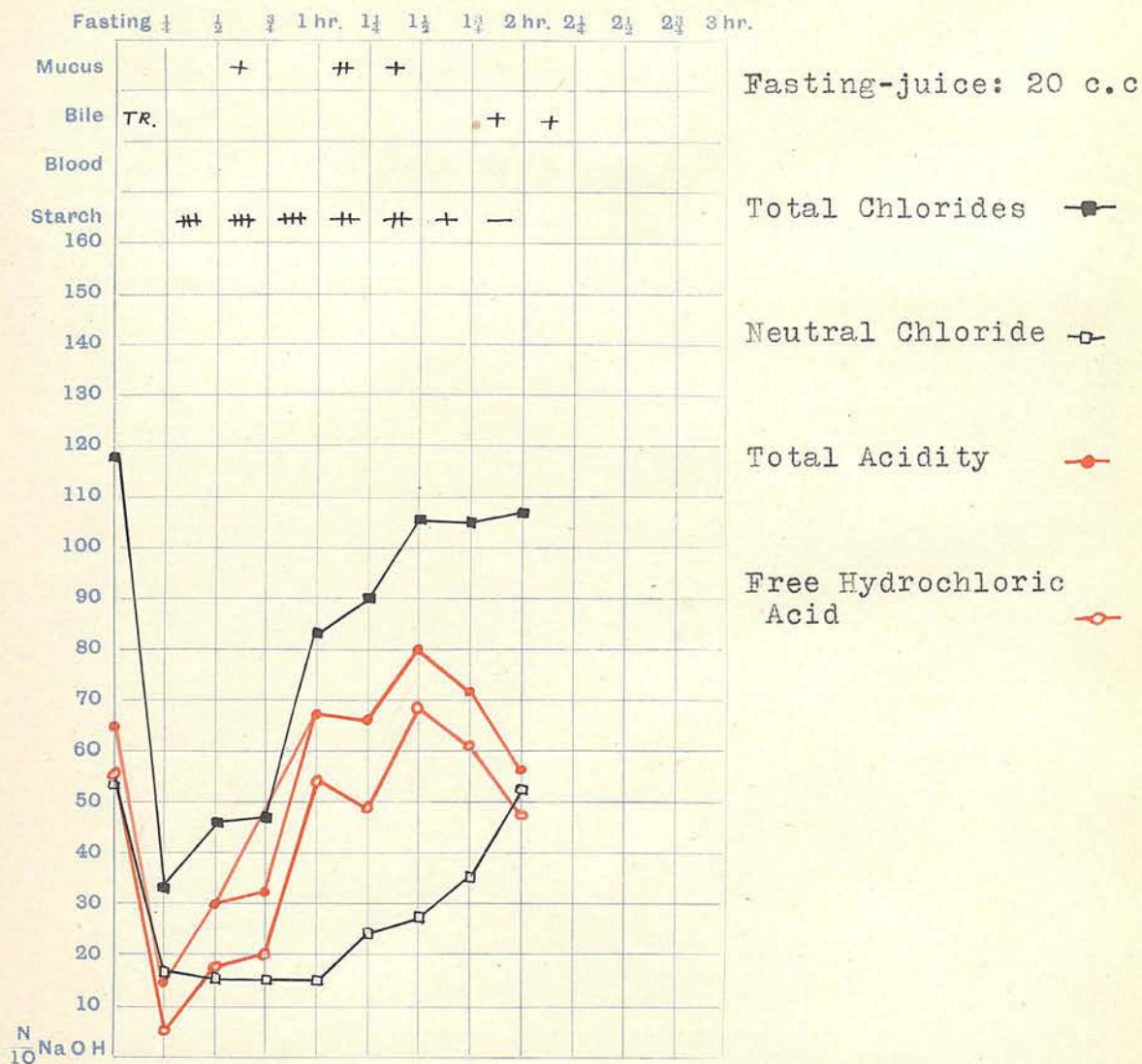
1. FRACTIONAL TEST-MEAL. Date 9. 5. '28.



Gastric ulcer (non-operated).

Name of Patient UV 8. (M. aet. 34)

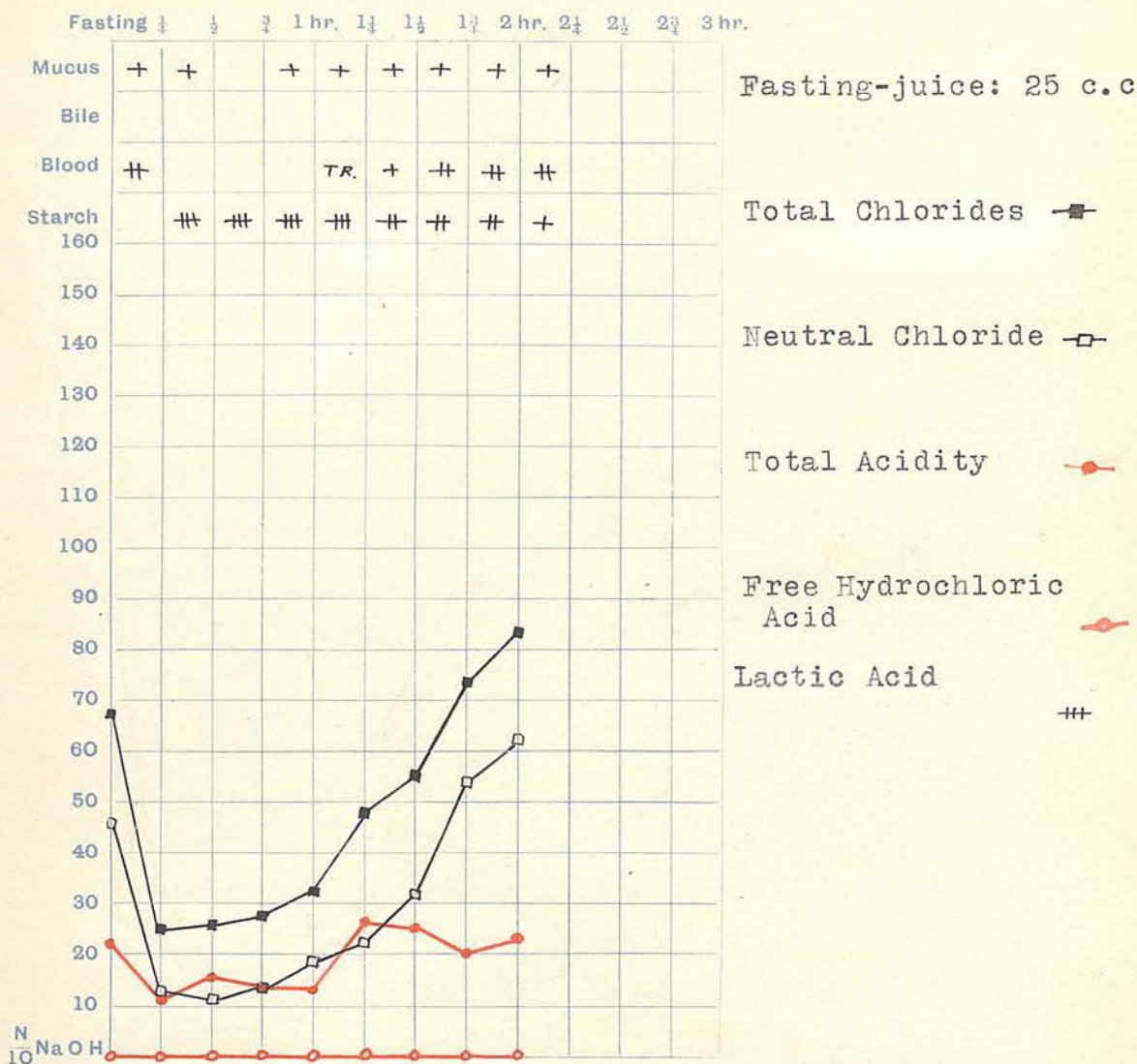
1. FRACTIONAL TEST-MEAL. Date 5. 6. '28.



Gastric ulcer (non-operated).

Name of Patient CV 1. (F. aet. 62)

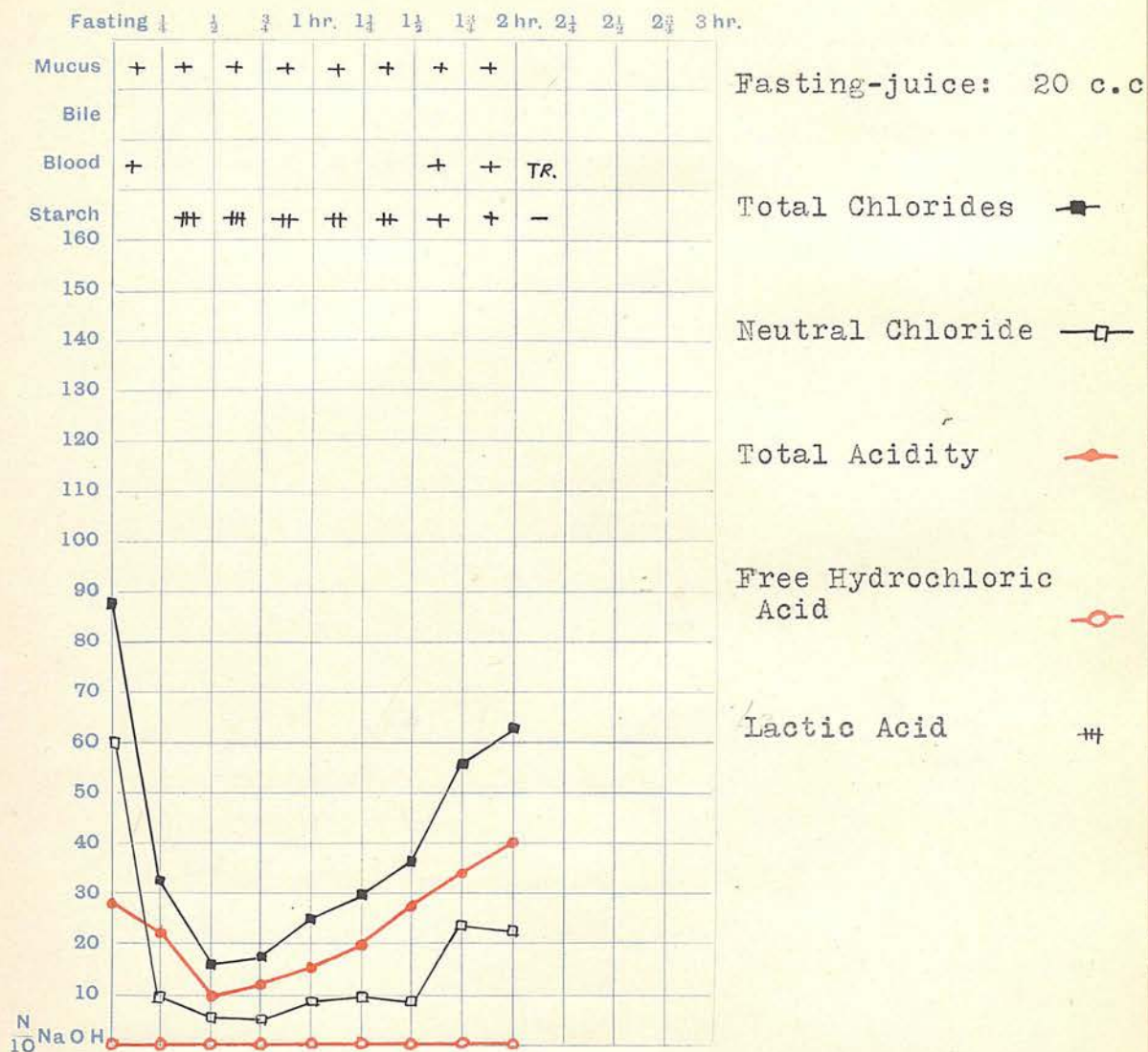
1. FRACTIONAL TEST-MEAL. Date 24. 7. '28.



Carcinoma of body of stomach.

Name of Patient CV 2. (M. aet. 66)

1. FRACTIONAL TEST-MEAL. Date 4. 3. '29

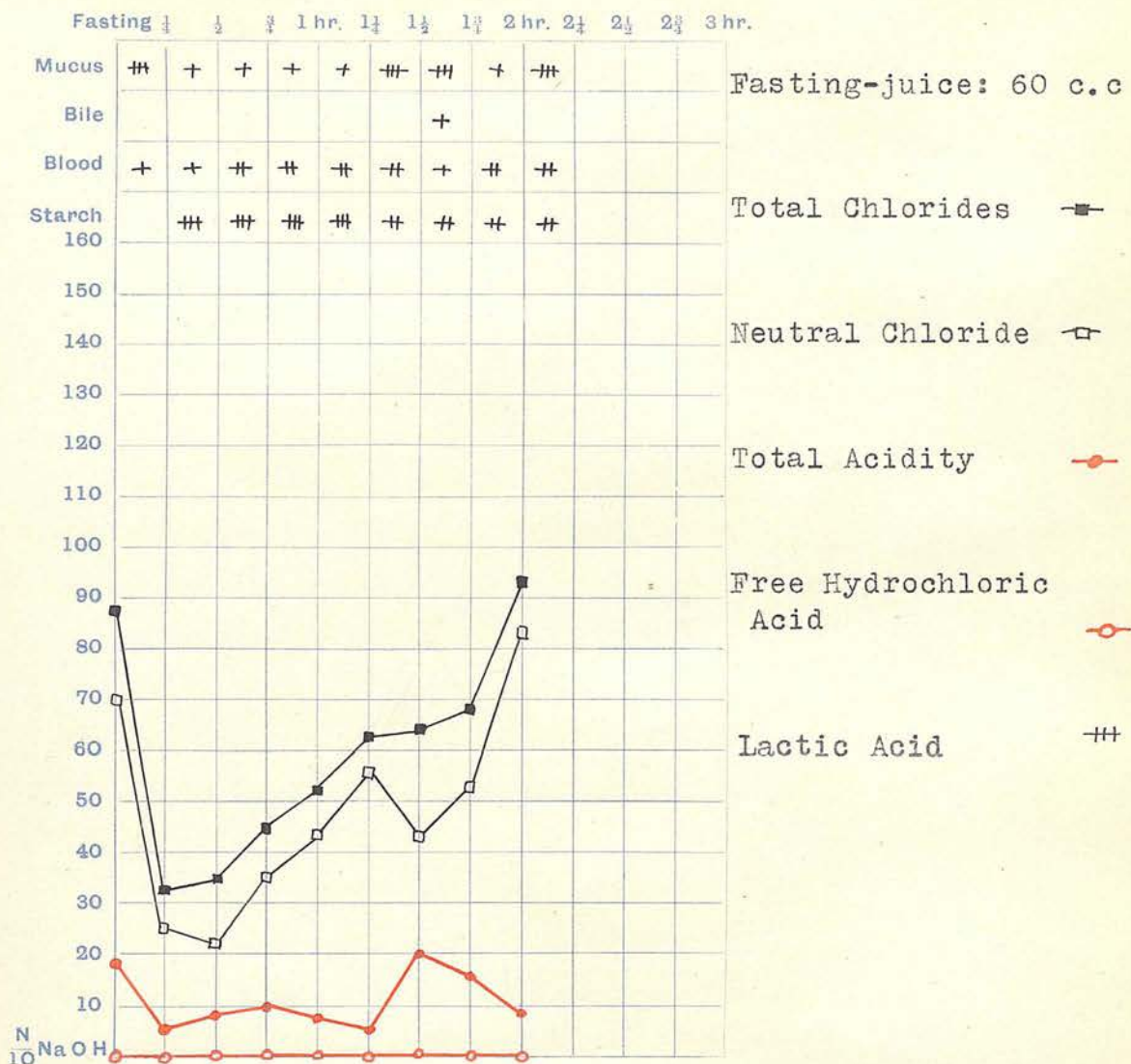


Carcinoma of body of stomach.

Name of Patient CV 3. (M. aet. 58)

1. FRACTIONAL TEST-MEAL.

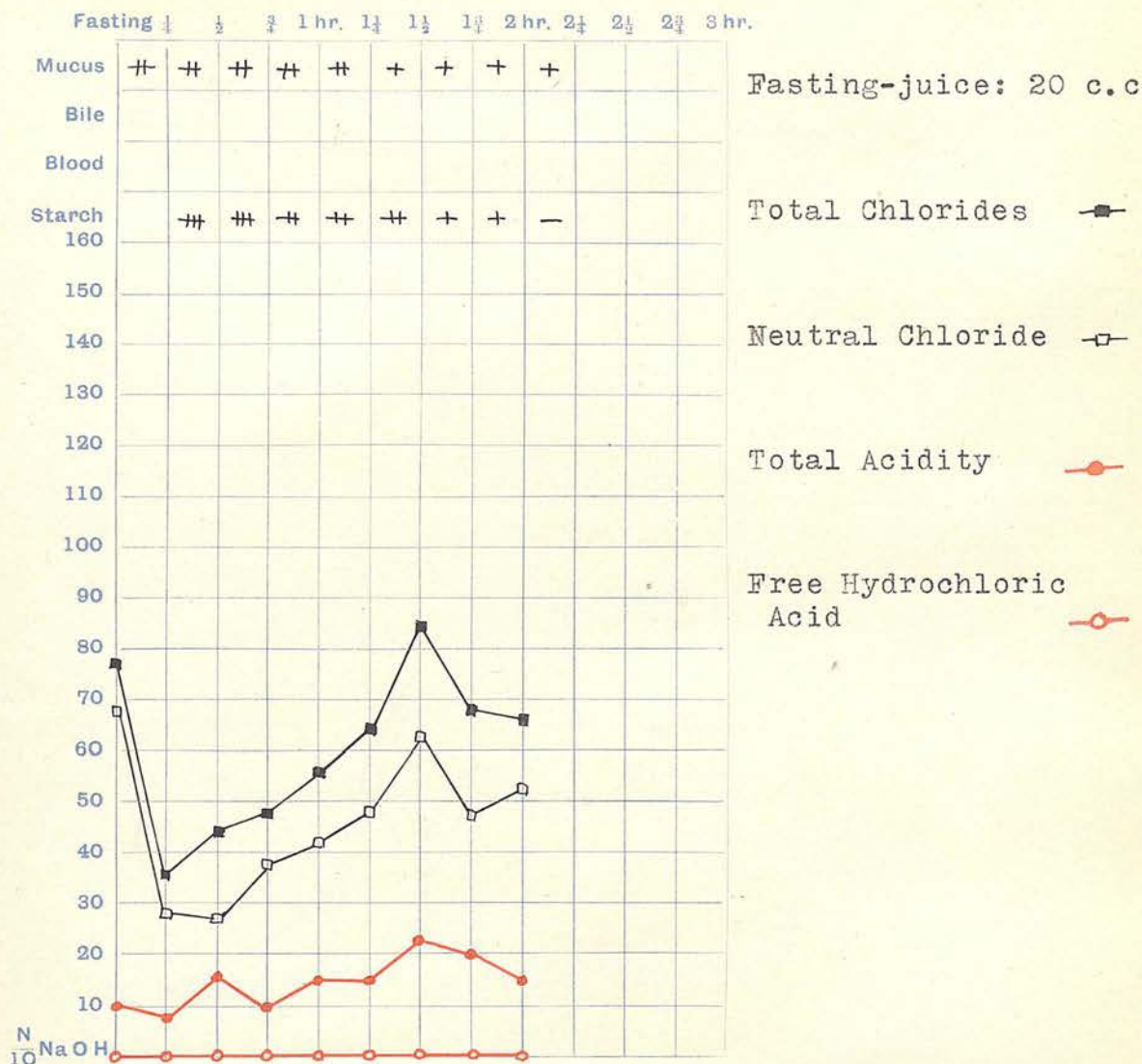
Date 29. 5. '29.



Carcinoma of stomach (non-operated).

Name of Patient G 1. (F. aet. 42)

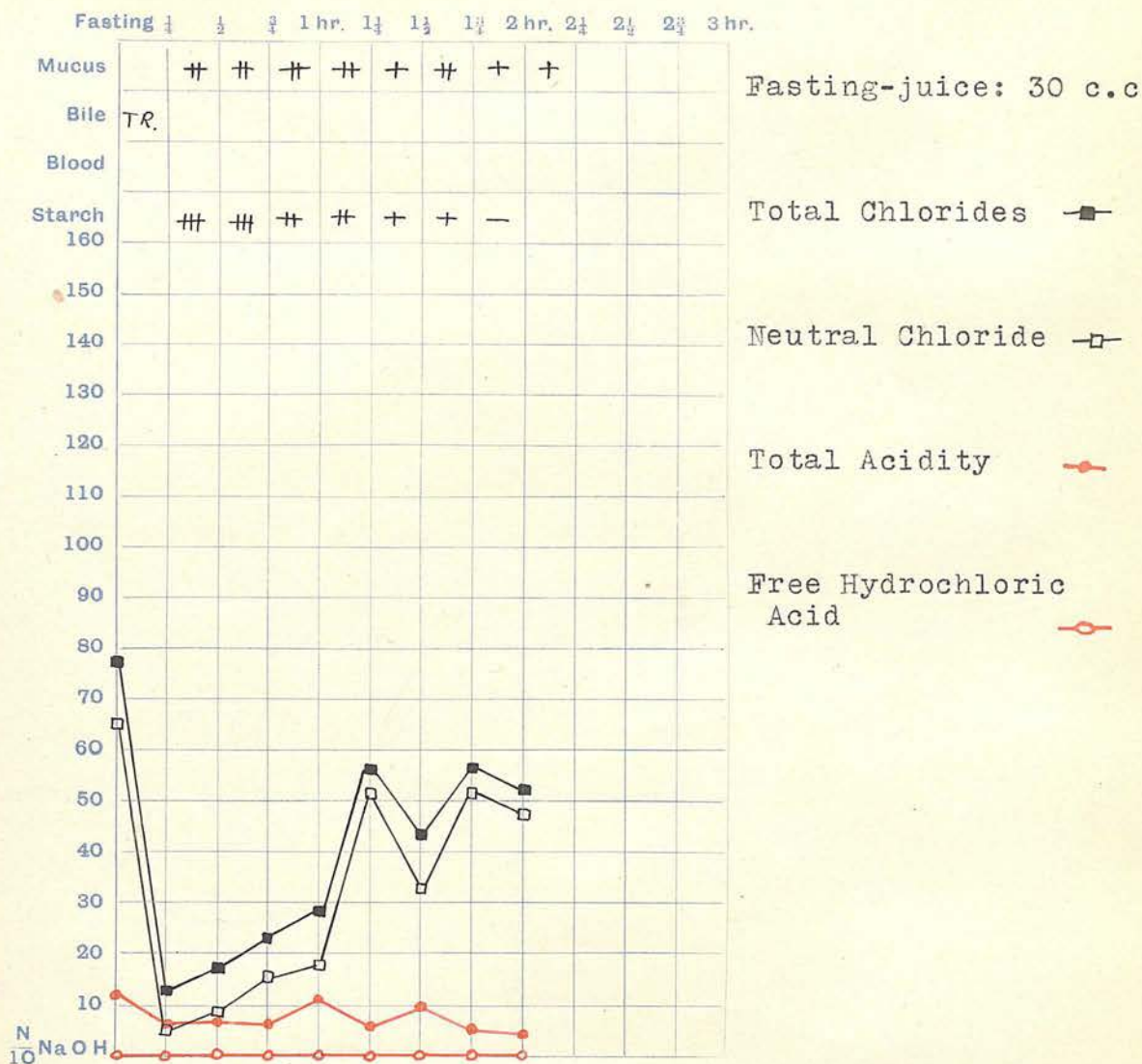
1. FRACTIONAL TEST-MEAL. Date 15. 6. '28.



Chronic primary gastritis.

Name of Patient G 2. (M. aet. 48)

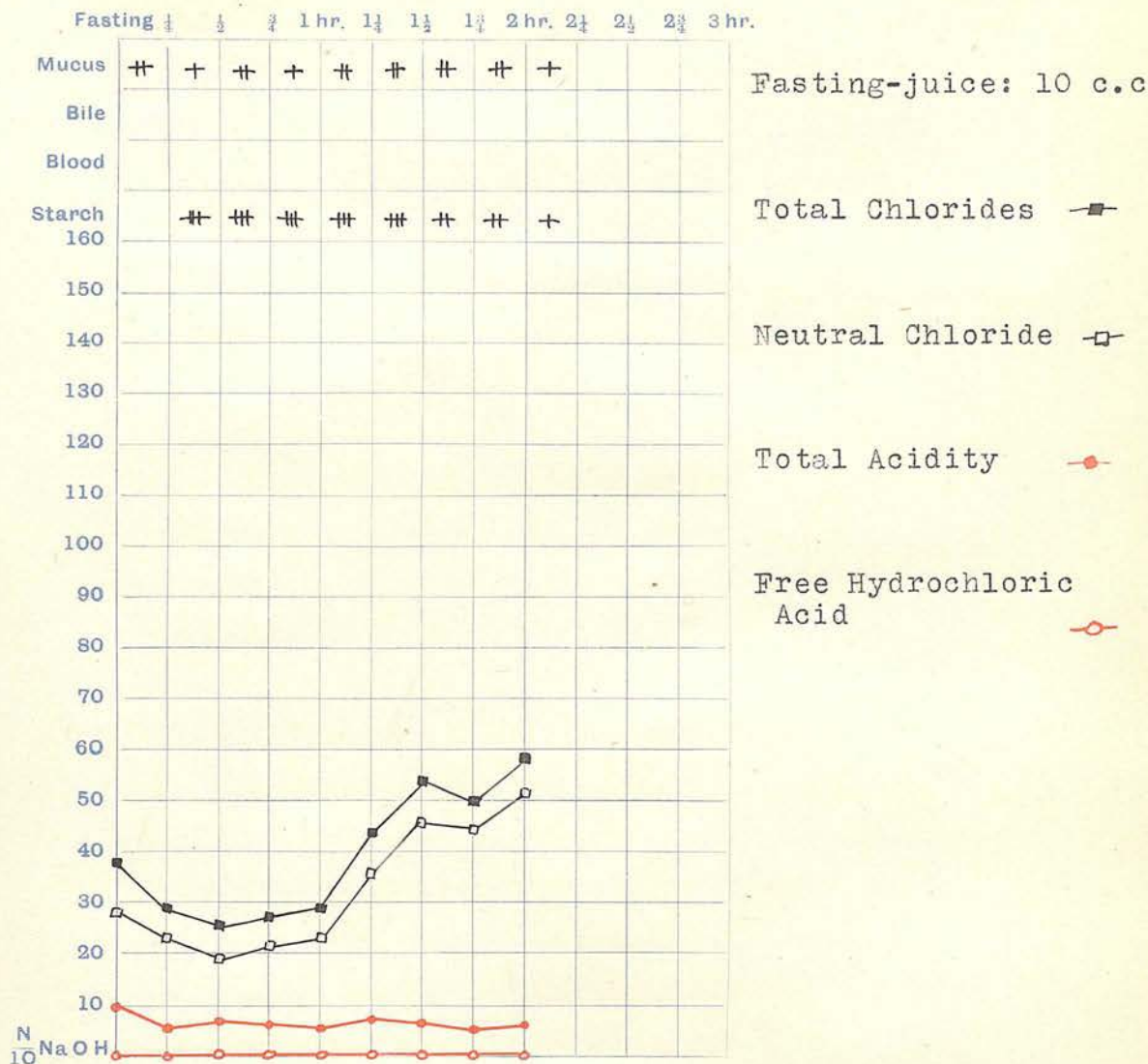
1. FRACTIONAL TEST-MEAL. Date 31. 5. '28.



Chronic primary gastritis.

Name of Patient G. 3.(A) (M. aet. 58)

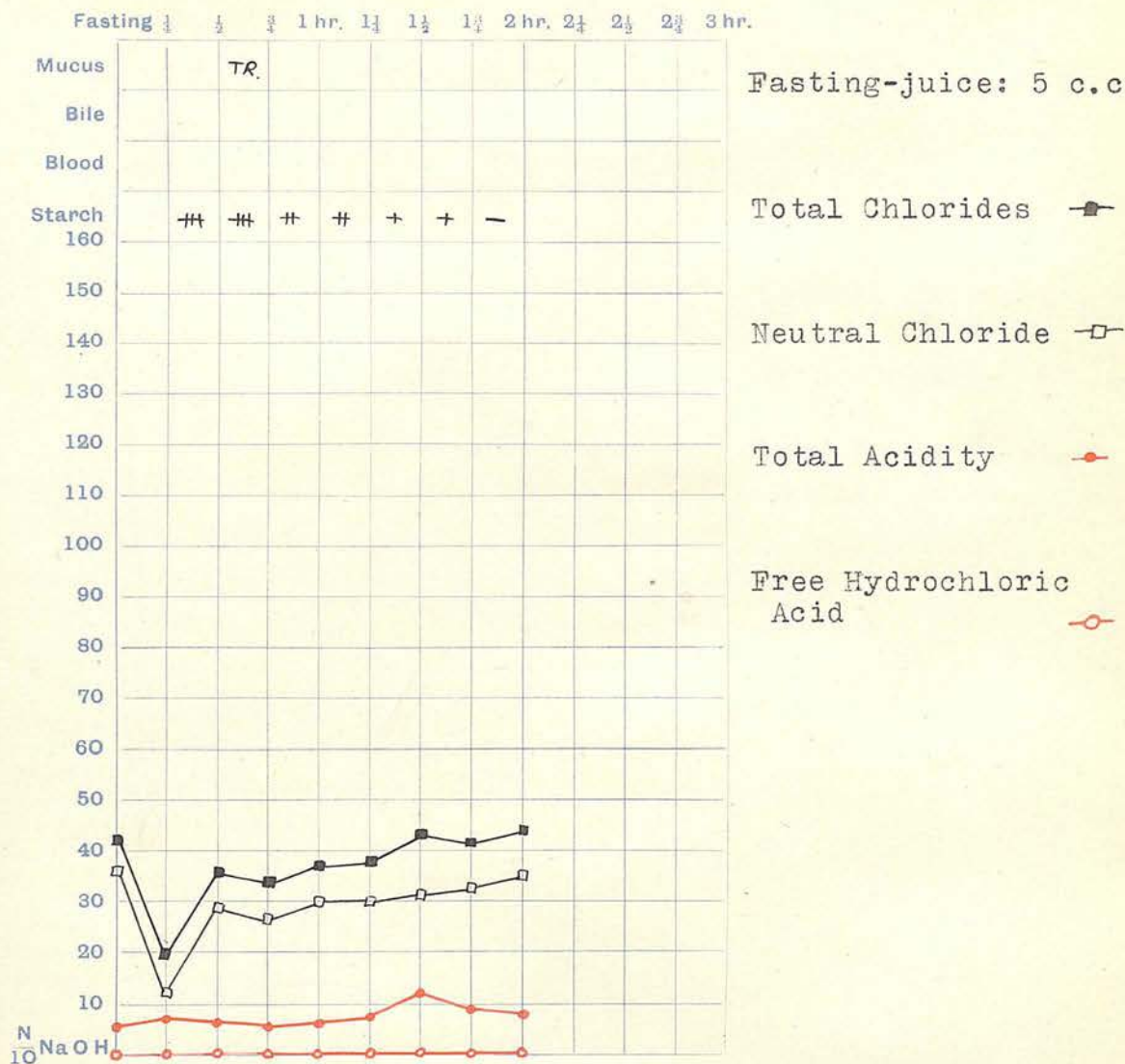
1. FRACTIONAL TEST-MEAL. Date 16. 6. '28.



Chronic primary gastritis.

Name of Patient G 3.(B) (M. aet. 58)

1. FRACTIONAL TEST-MEAL. Date 23. 6. '28.

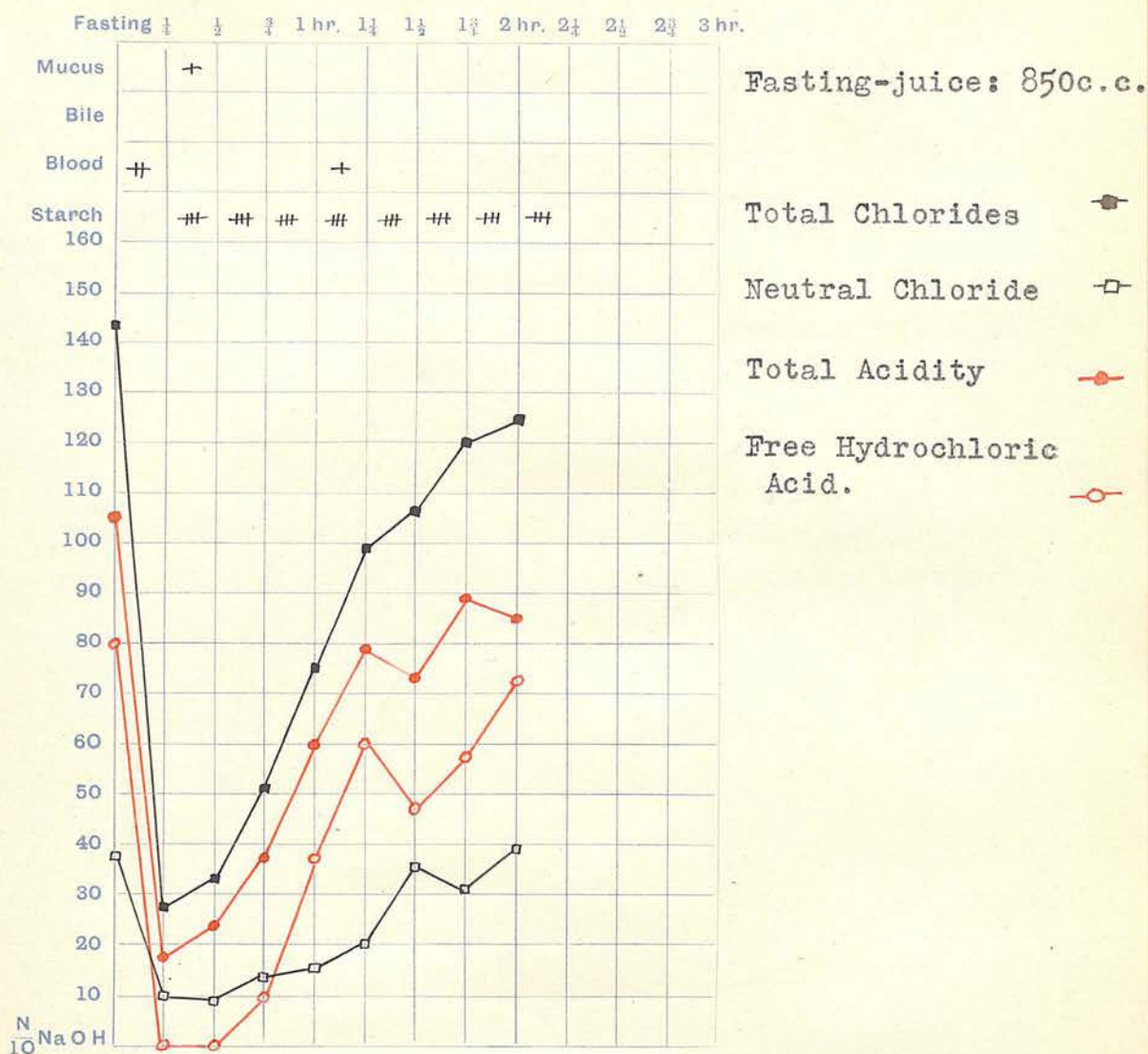


After one week's medical treatment.

Note marked decrease of mucus.

Name of Patient UD 1(A) (M. aet. 53)

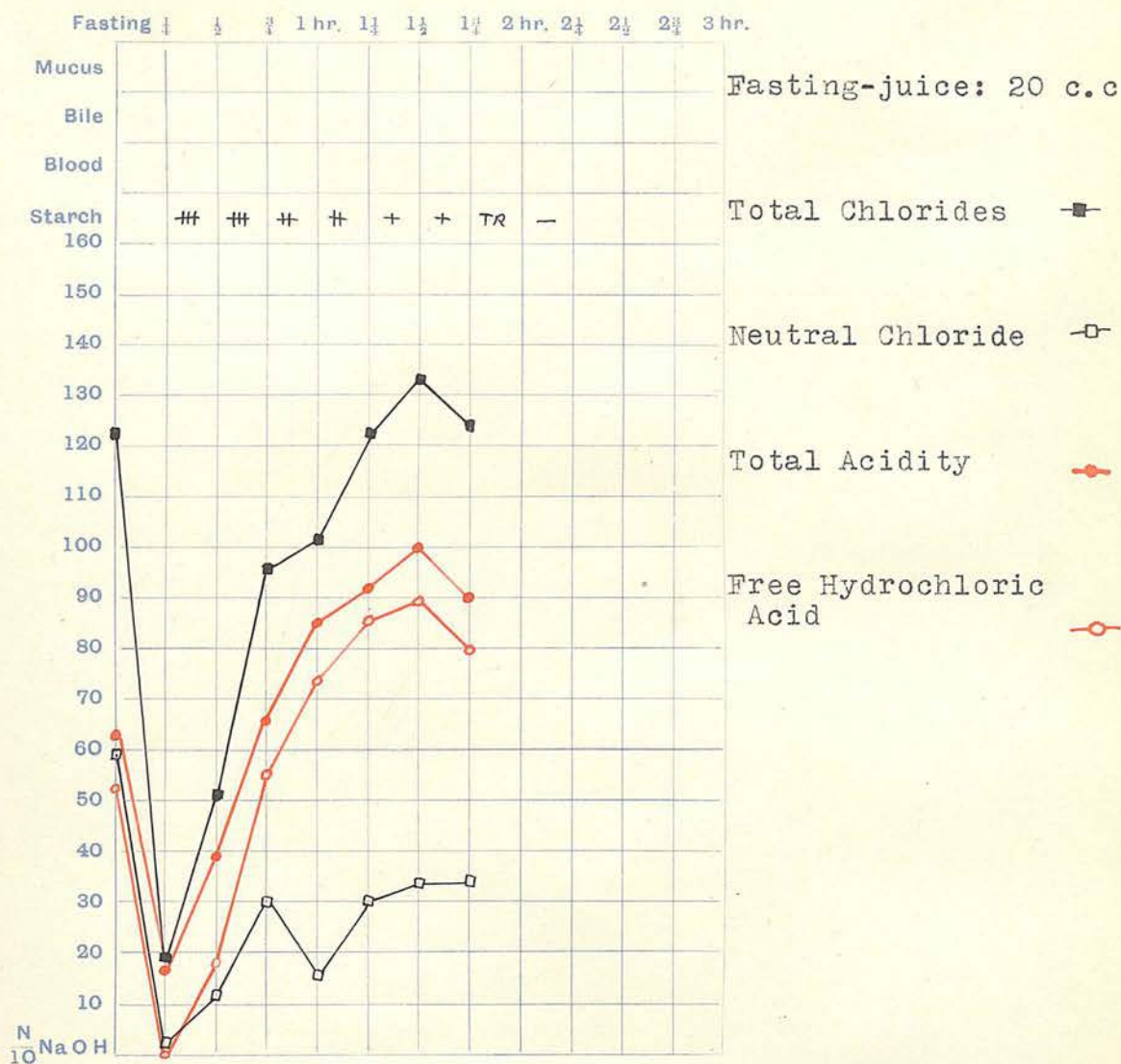
1. FRACTIONAL TEST-MEAL. Date 22. 2. '29.



Chronic duodenal ulcer - on admission.

Name of Patient UD 1.(B) (M. aet. 53)

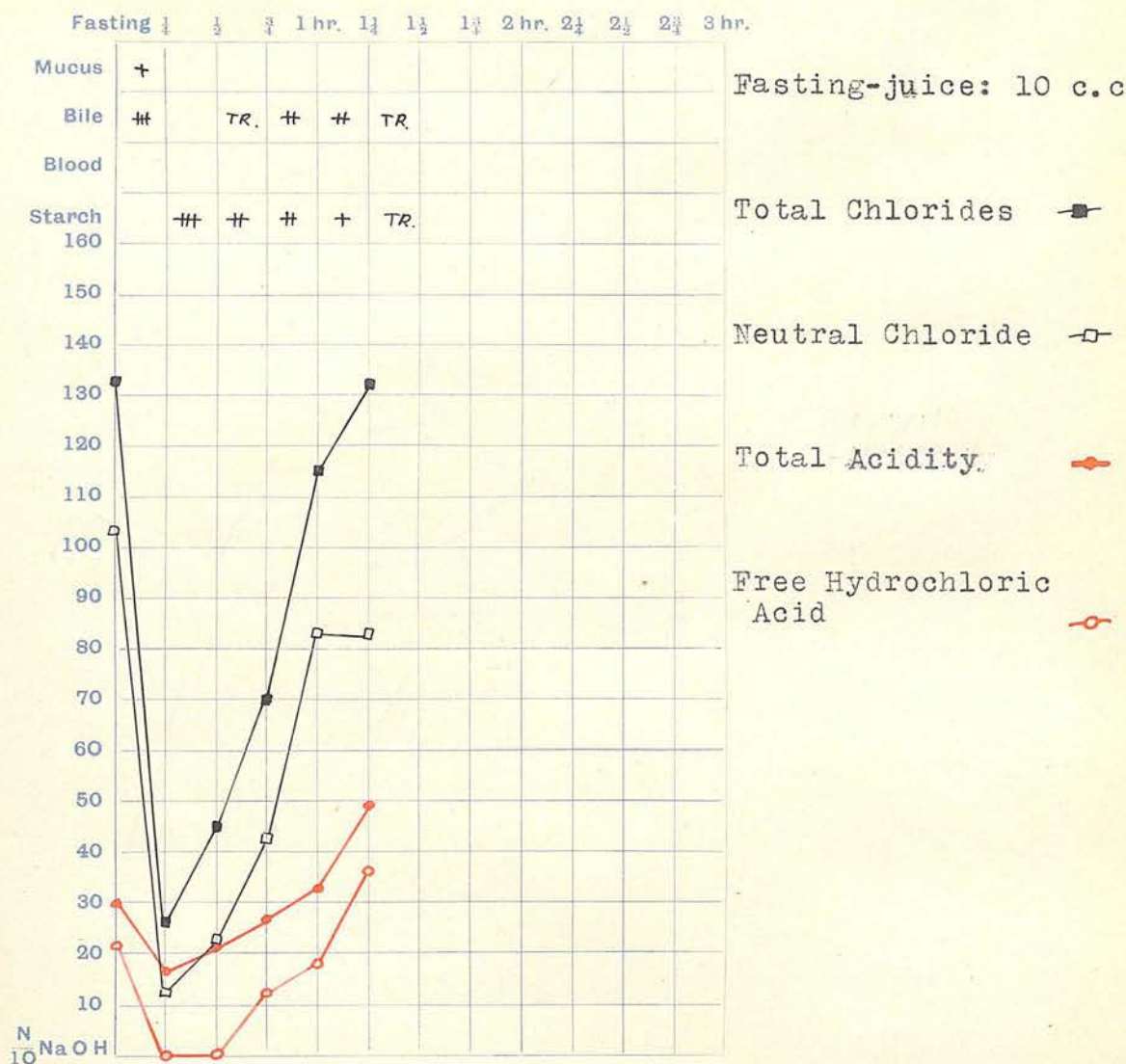
1. FRACTIONAL TEST-MEAL. Date 4. 3. '29.



After ten days' medical treatment.

Note decrease of fasting-juice volume.

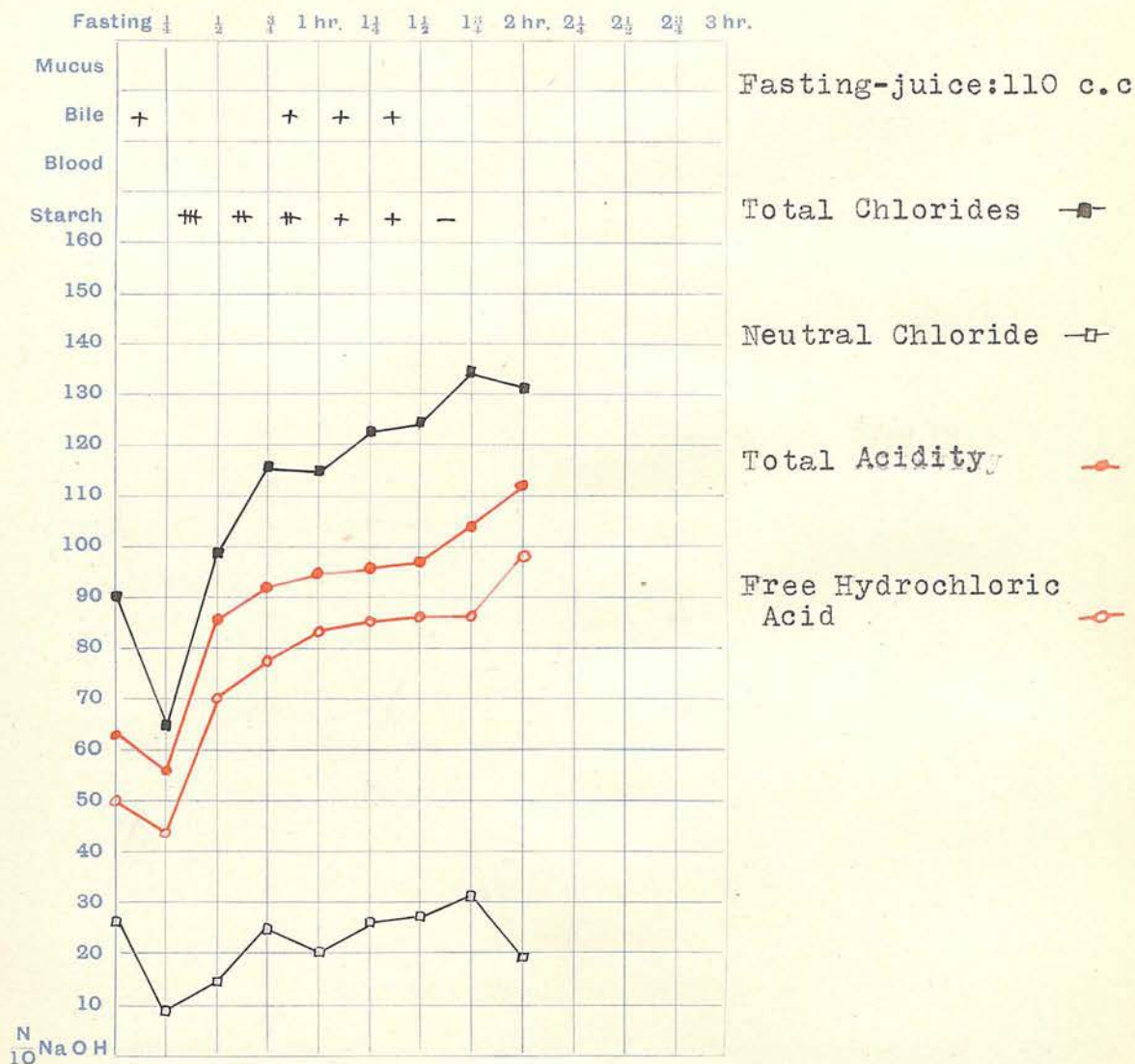
1. FRACTIONAL TEST-MEAL. Date 19. 3. '29.



Two weeks after gastroenterostomy.

Name of Patient UD 2.(A) (M. aet. 45)

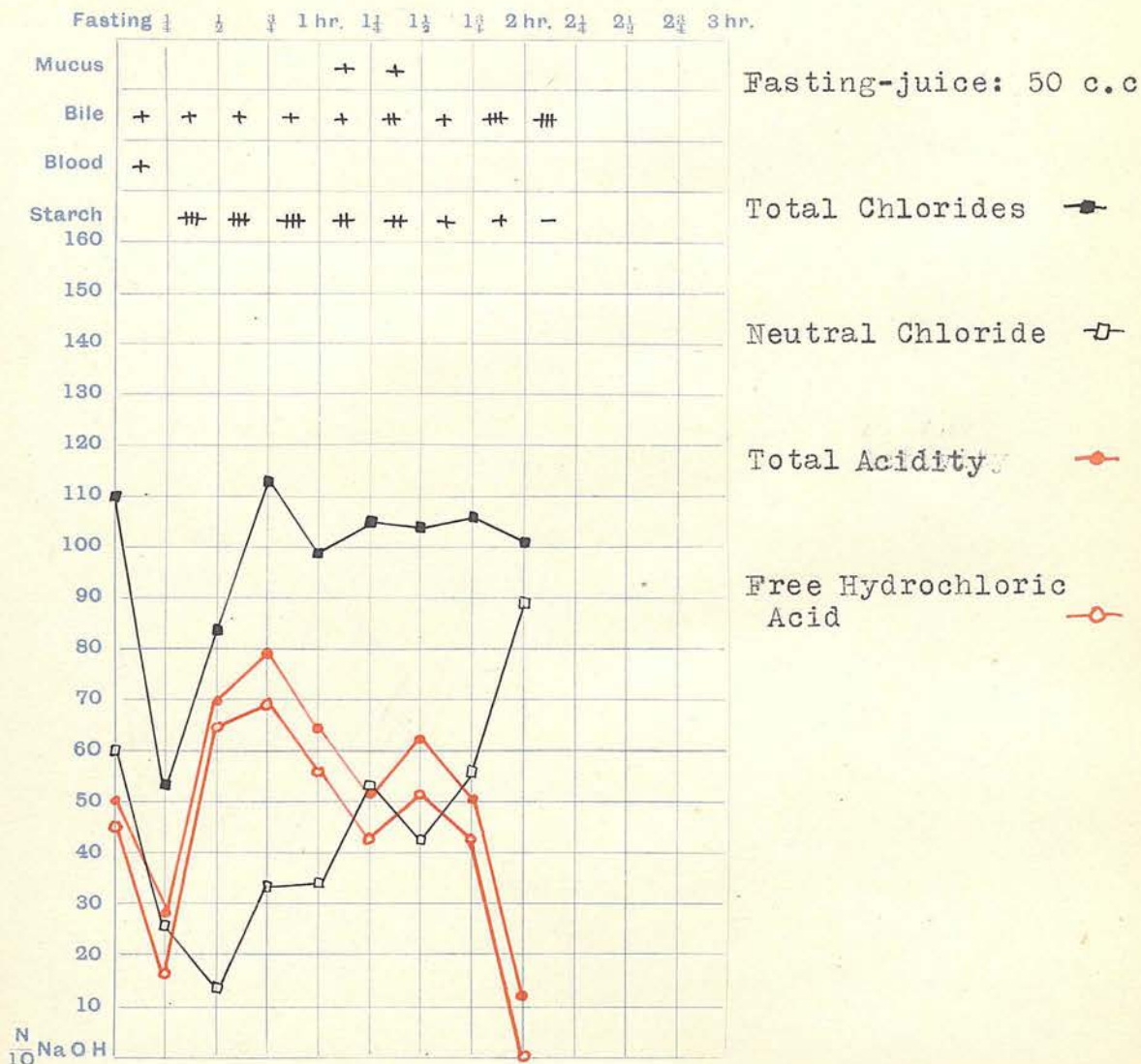
1. FRACTIONAL TEST-MEAL. Date 3. 5. '29.



Chronic duodenal ulcer, preoperative.

Name of Patient UD 2.(B) (M. aet. 45)

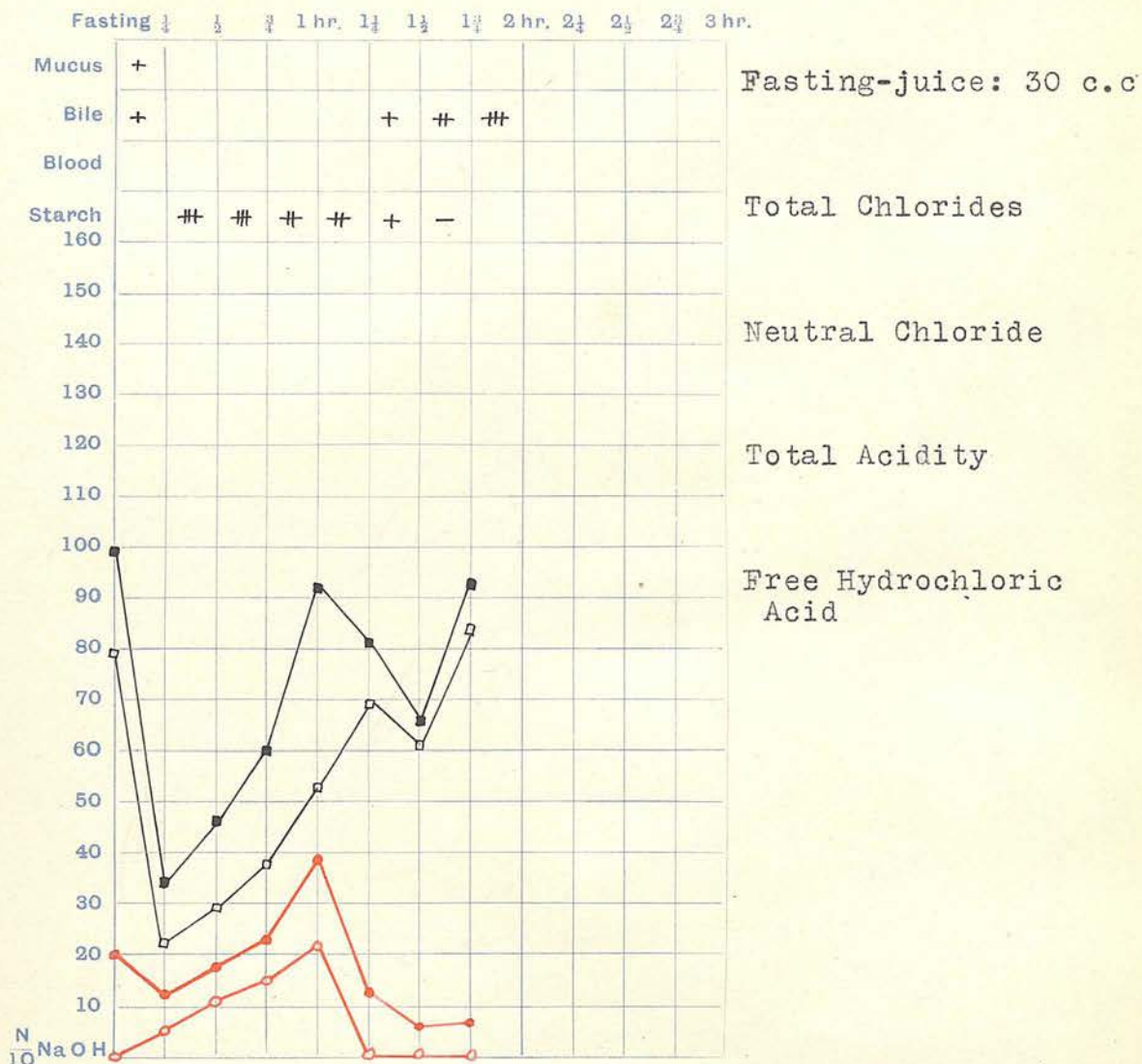
1. FRACTIONAL TEST-MEAL. Date 25. 5. '29.



Three weeks after gastroenterostomy.

Name of Patient UD 3.(A) (M. aet. 46)

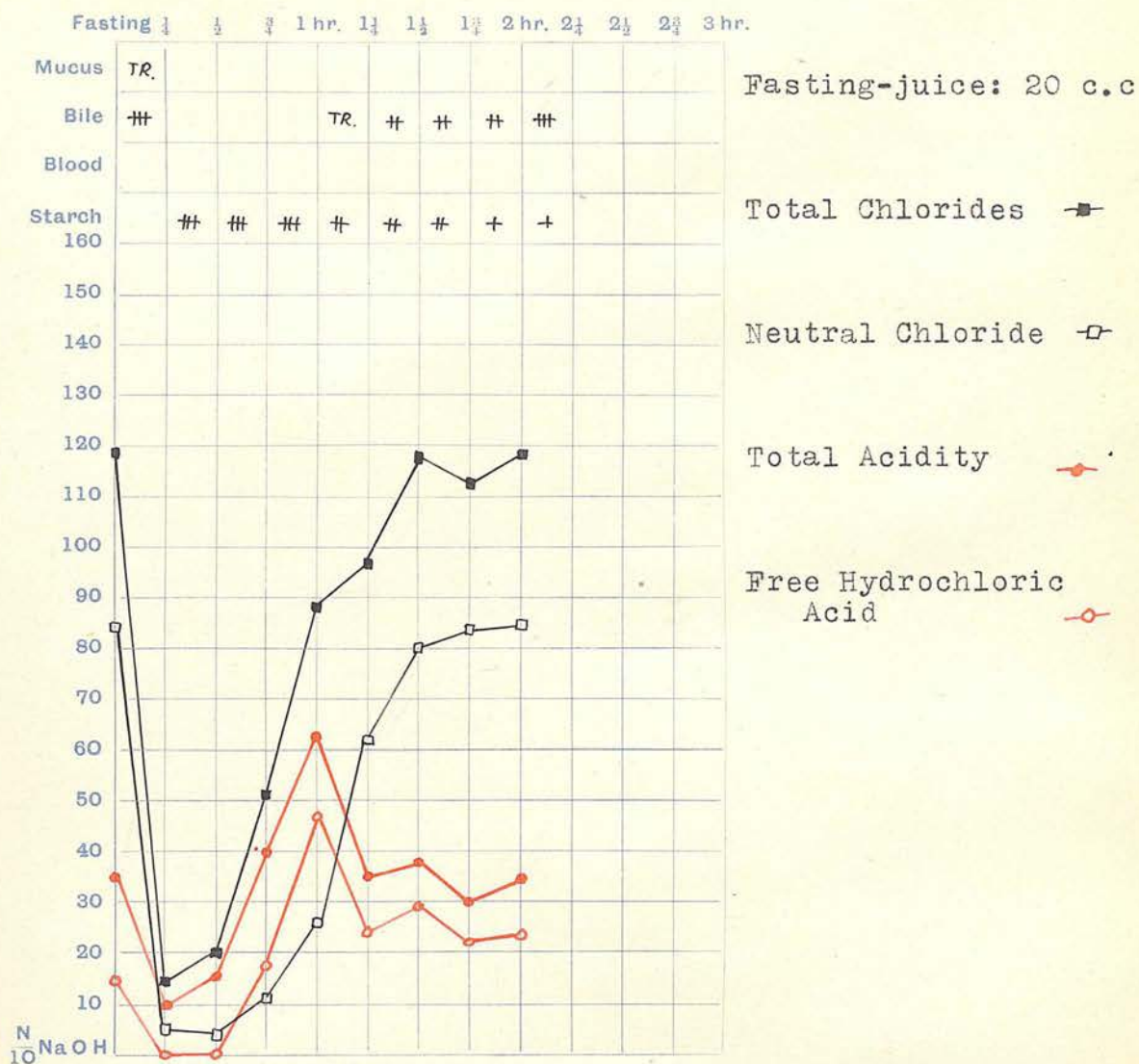
1. FRACTIONAL TEST-MEAL. Date 10. 2. '29.



Chronic duodenal ulcer, preoperative.

Name of Patient UD 3.(B) (M. aet. 46)

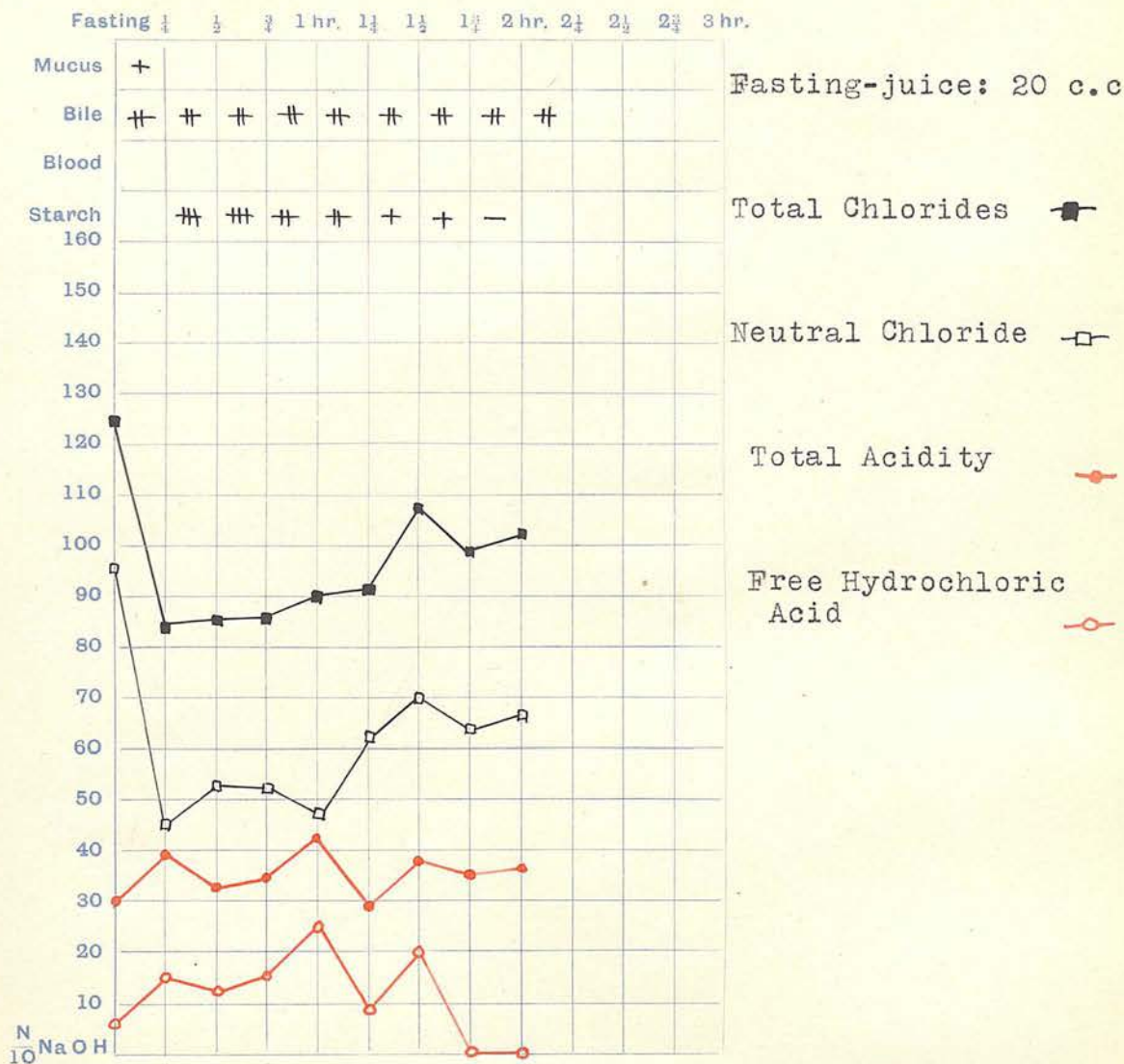
1. FRACTIONAL TEST-MEAL. Date 4. 3. '29.



Three weeks after gastroenterostomy.

Name of Patient UD 4.(A) (M. aet. 49)

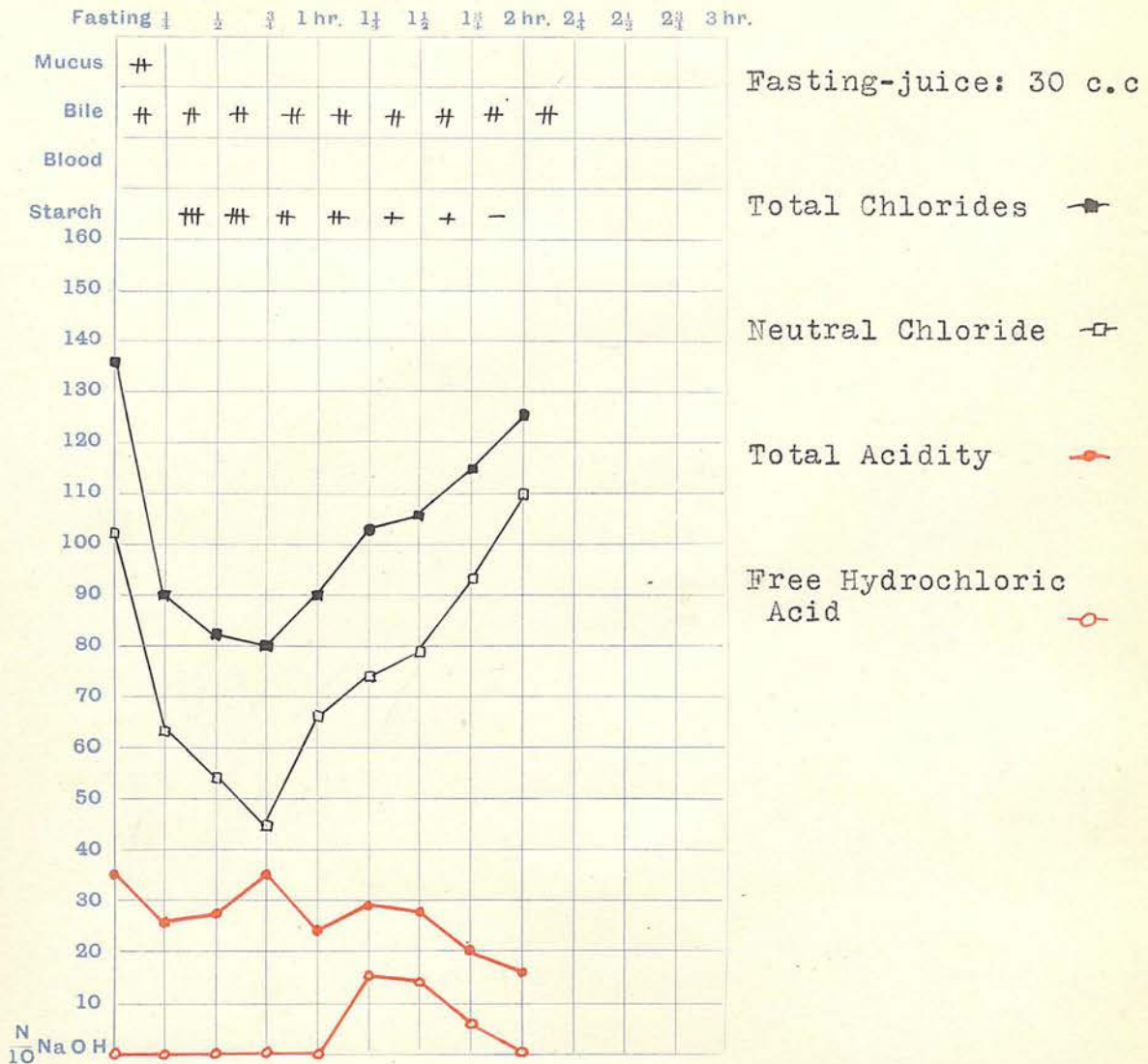
1. FRACTIONAL TEST-MEAL. Date 16. 5. '28.



Chronic duodenal ulcer, preoperative.

Name of Patient UD 4.(B) (M. aet. 49)

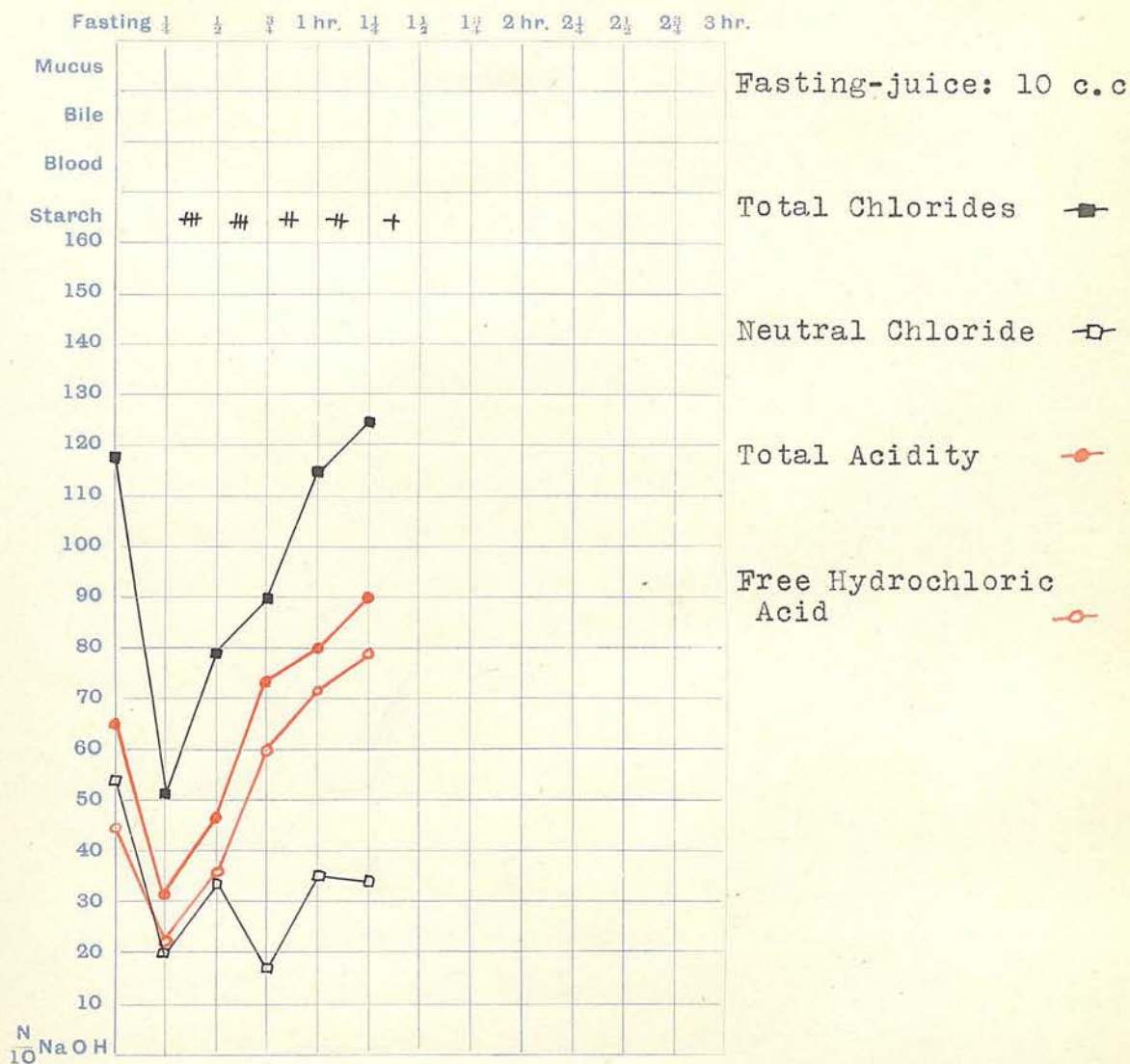
1. FRACTIONAL TEST-MEAL. Date 1. 6. '28.



Two weeks after gastroenterostomy.

Name of Patient UD 5.(A) (M. aet. 52)

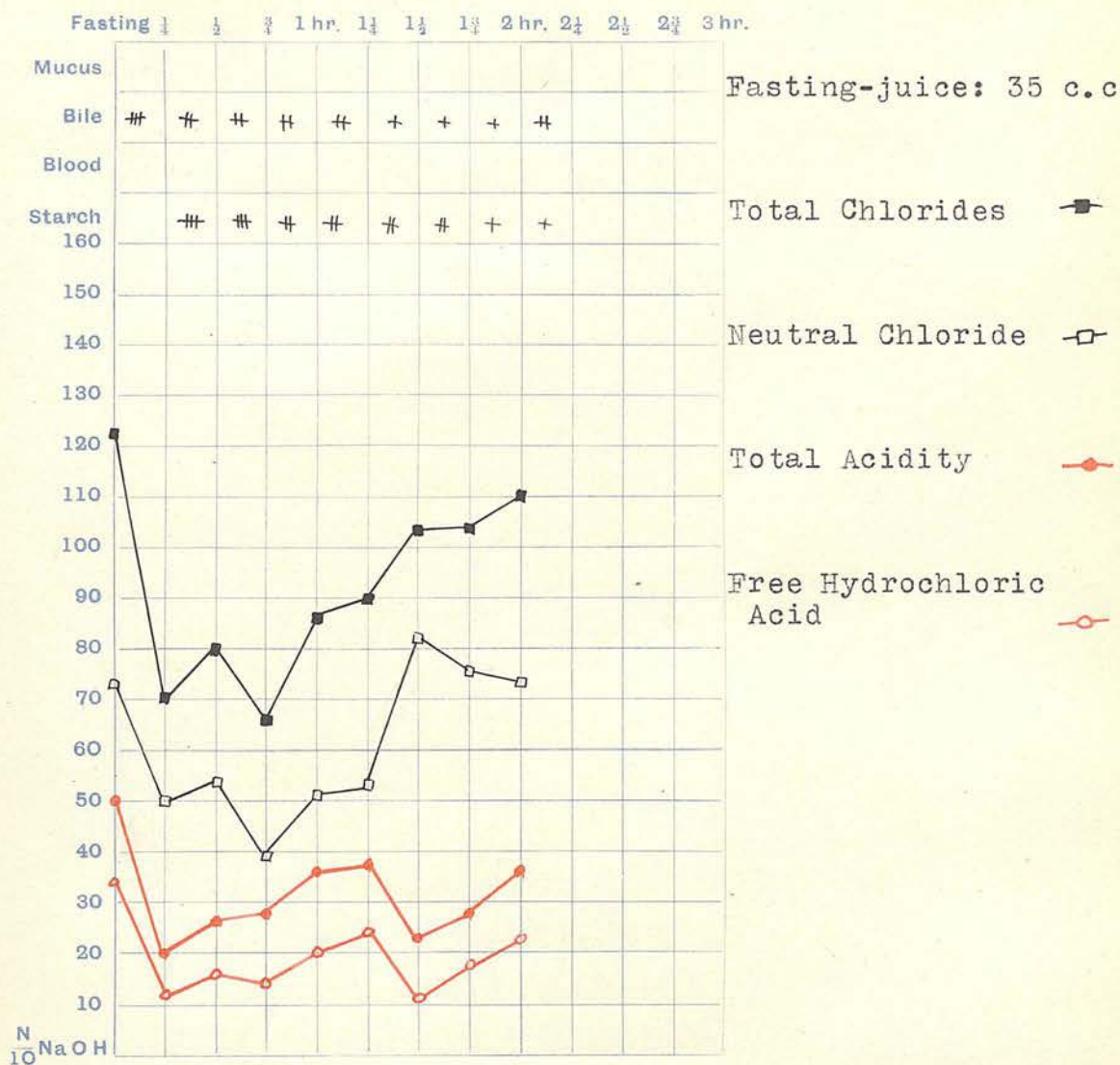
1. FRACTIONAL TEST-MEAL. Date 24. 3. '29.



Chronic duodenal ulcer, preoperative.

Name of Patient UD 5.(B) (M. aet. 52)

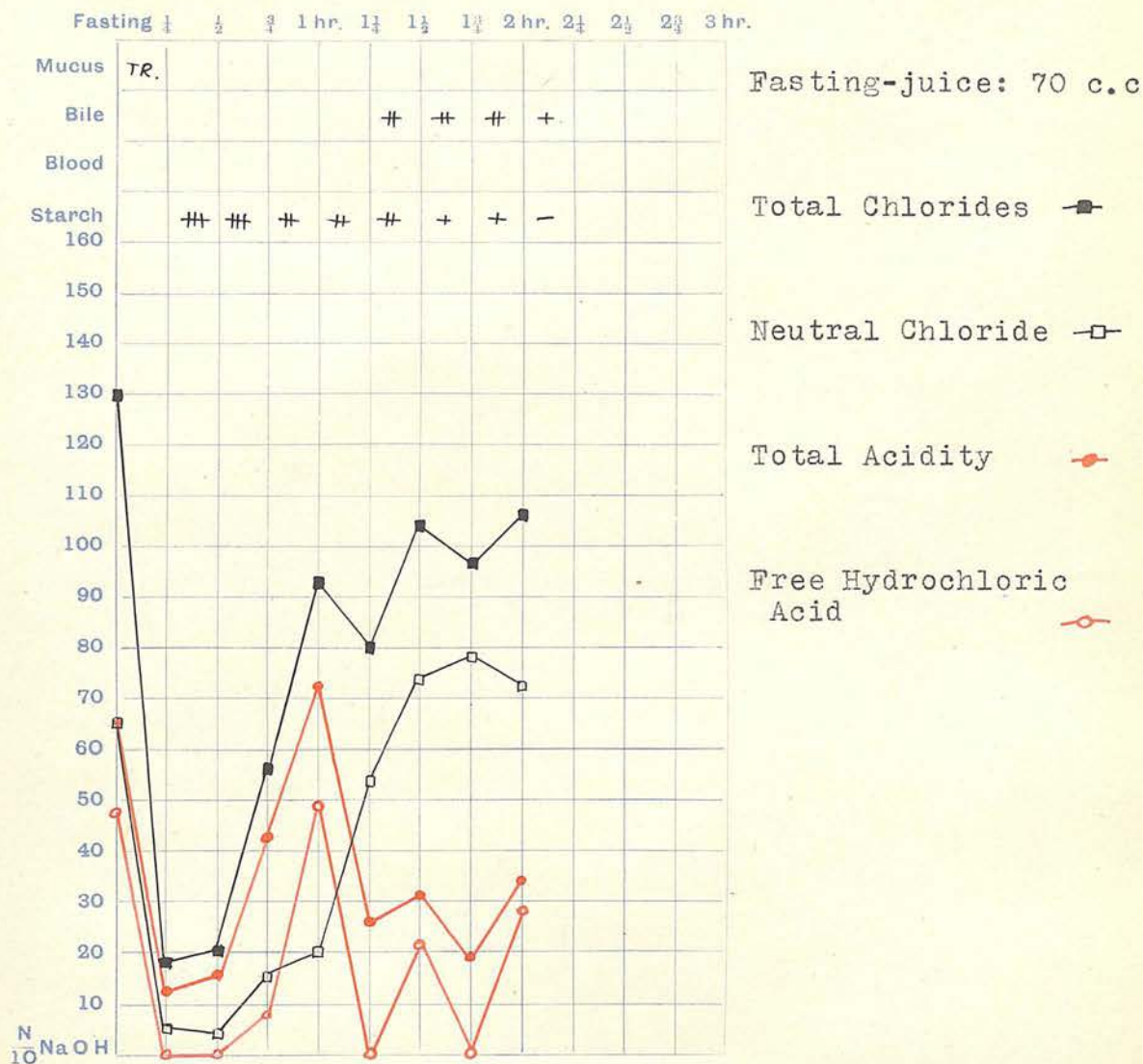
1. FRACTIONAL TEST-MEAL. Date 29. 4. '29.



Three weeks after gastroenterostomy.

Name of Patient UD 6.(A) (M. aet. 45)

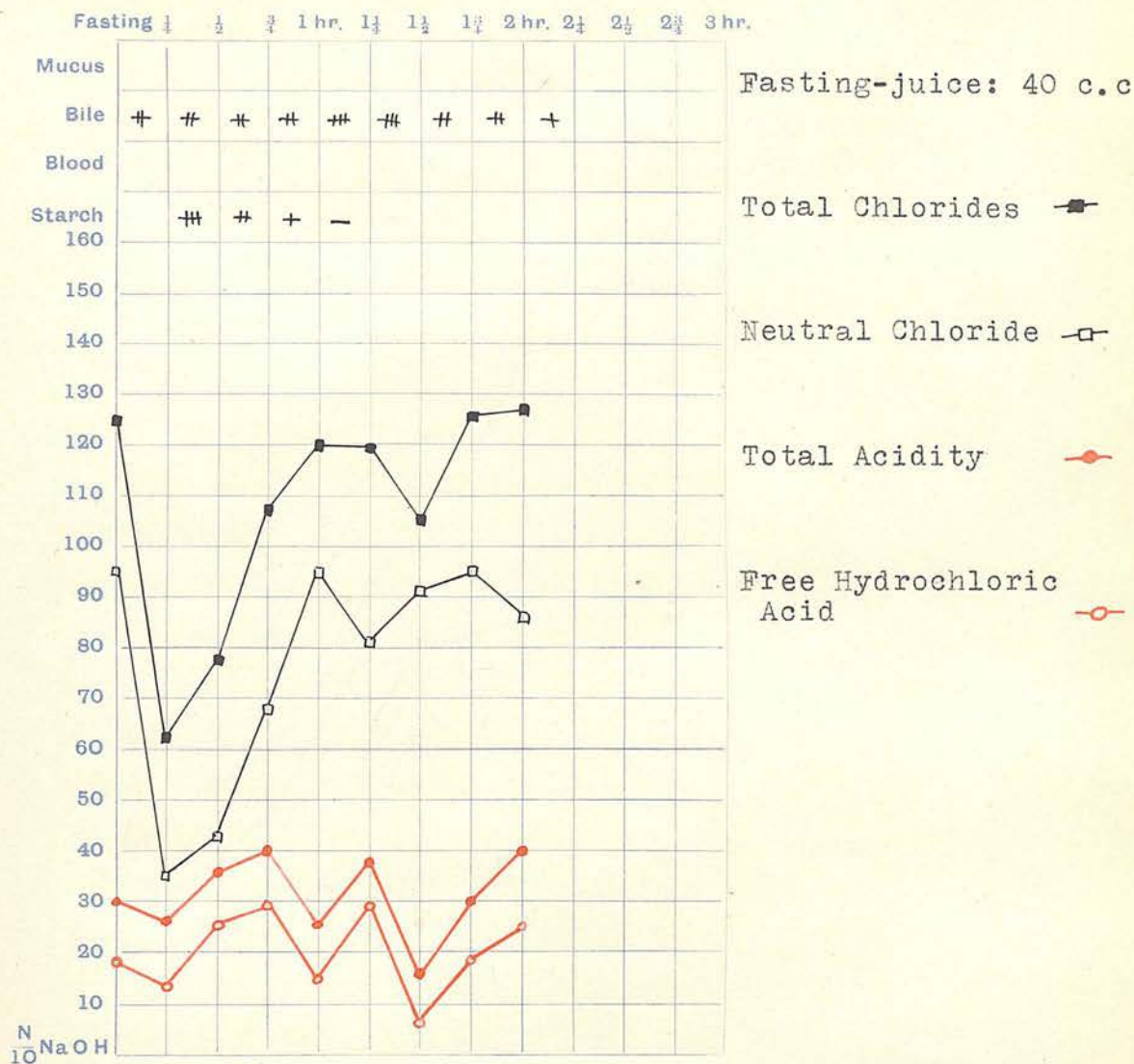
1. FRACTIONAL TEST-MEAL. Date 25. 5. '28.



Chronic duodenal ulcer, preoperative.

Name of Patient UD 6.(B) (M. aet. 45)

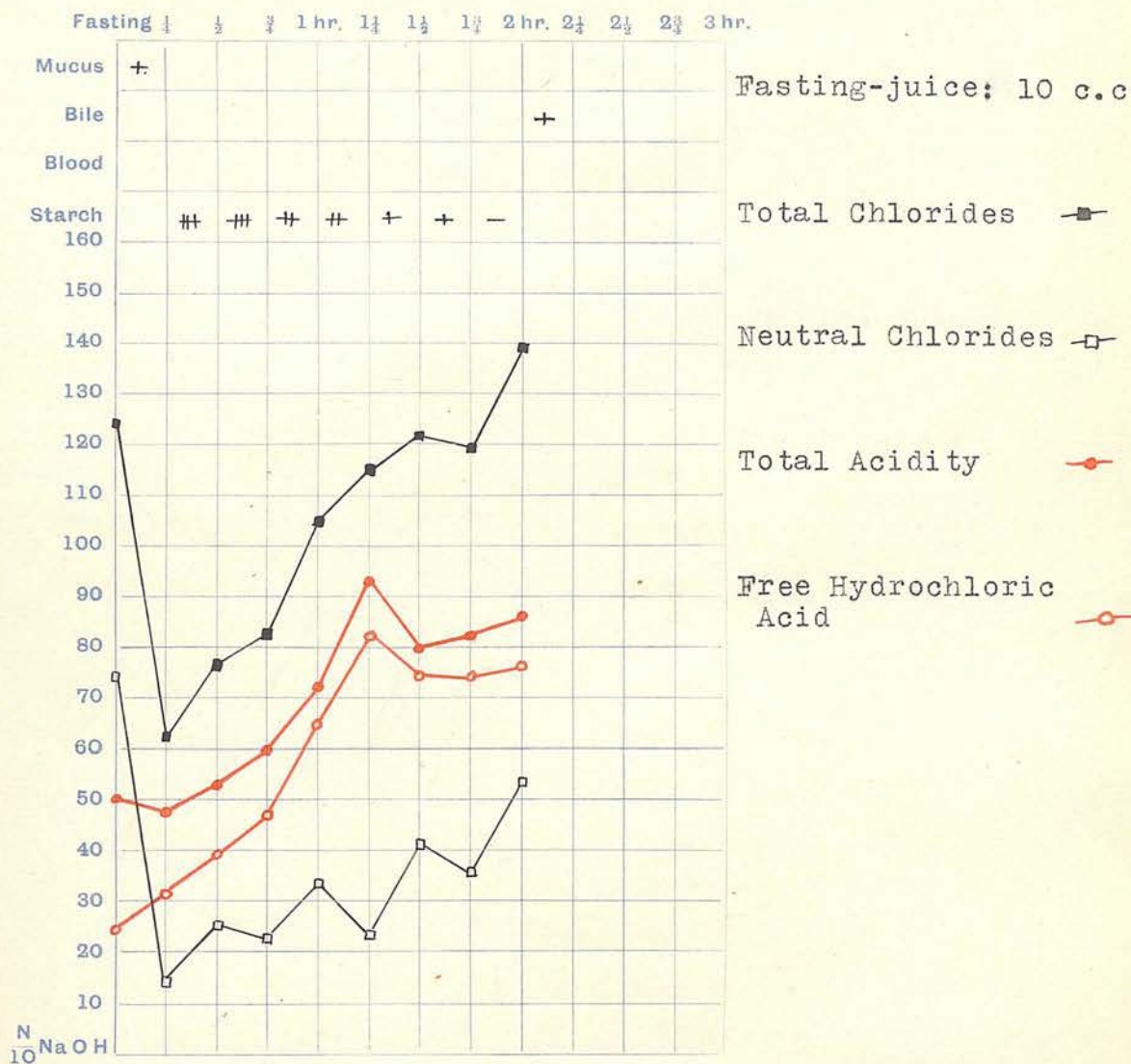
1. FRACTIONAL TEST-MEAL. Date 15. 6. '28.



Three weeks after gastroenterostomy.

Name of Patient UD 7. (M. aet. 36)

1. FRACTIONAL TEST-MEAL. Date 15. 3. '29.



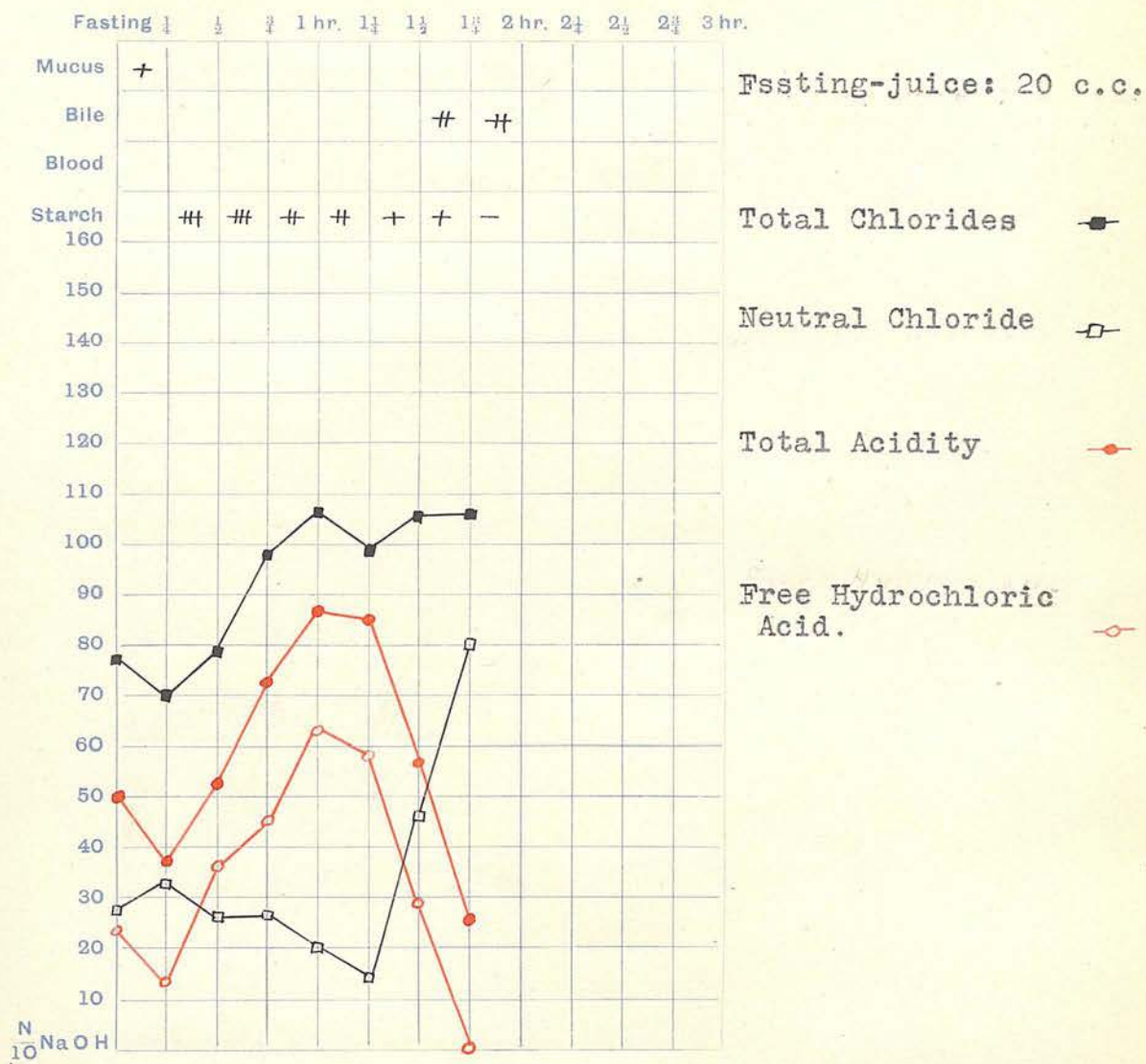
Chronic duodenal ulcer.

Name of Patient

UD 8. (M. aet. 54)

1. FRACTIONAL TEST-MEAL.

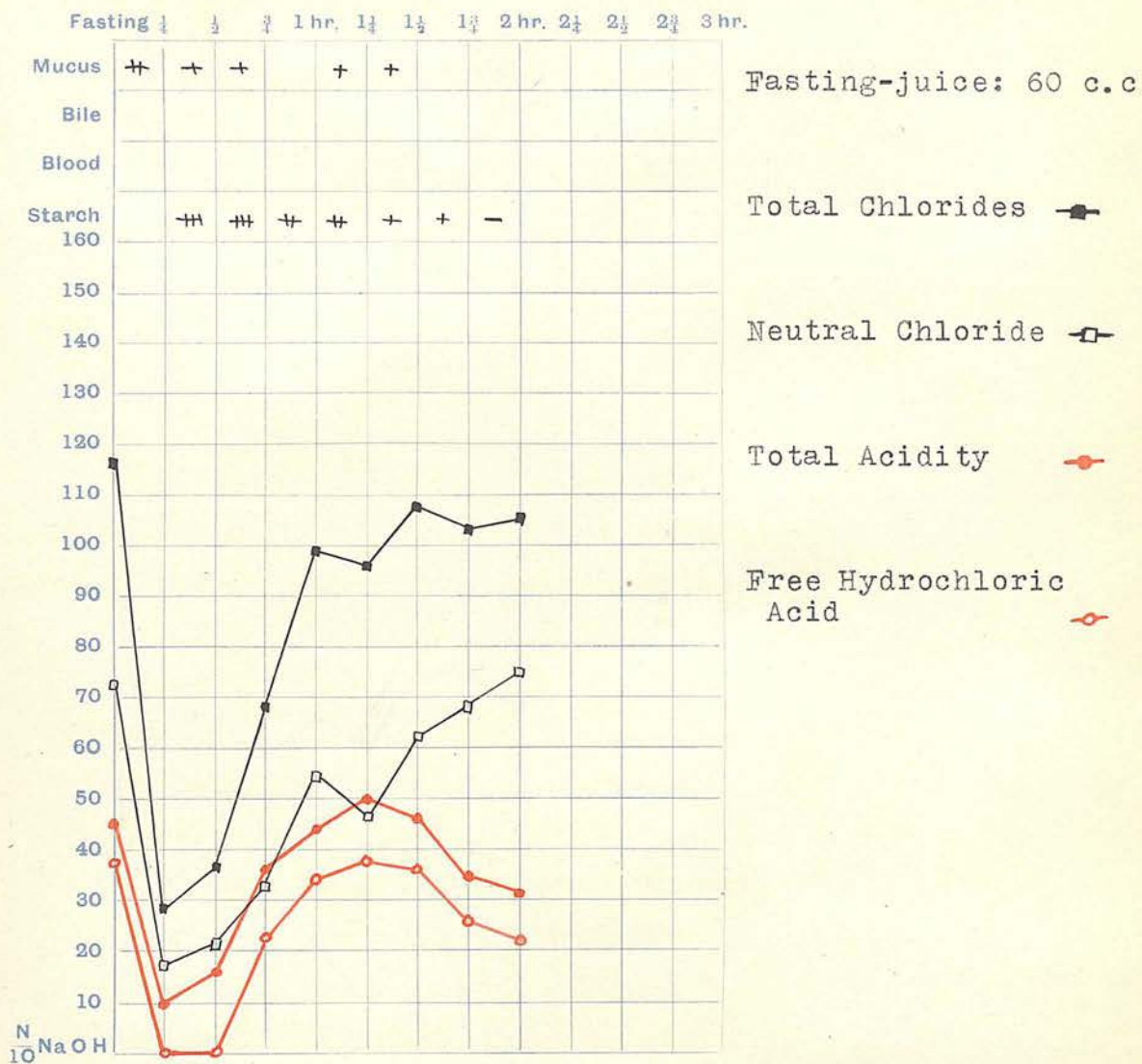
Date 25. 4. '28.



Chronic Duodenal Ulcer.

Name of Patient UD 9. (M. aet. 34)

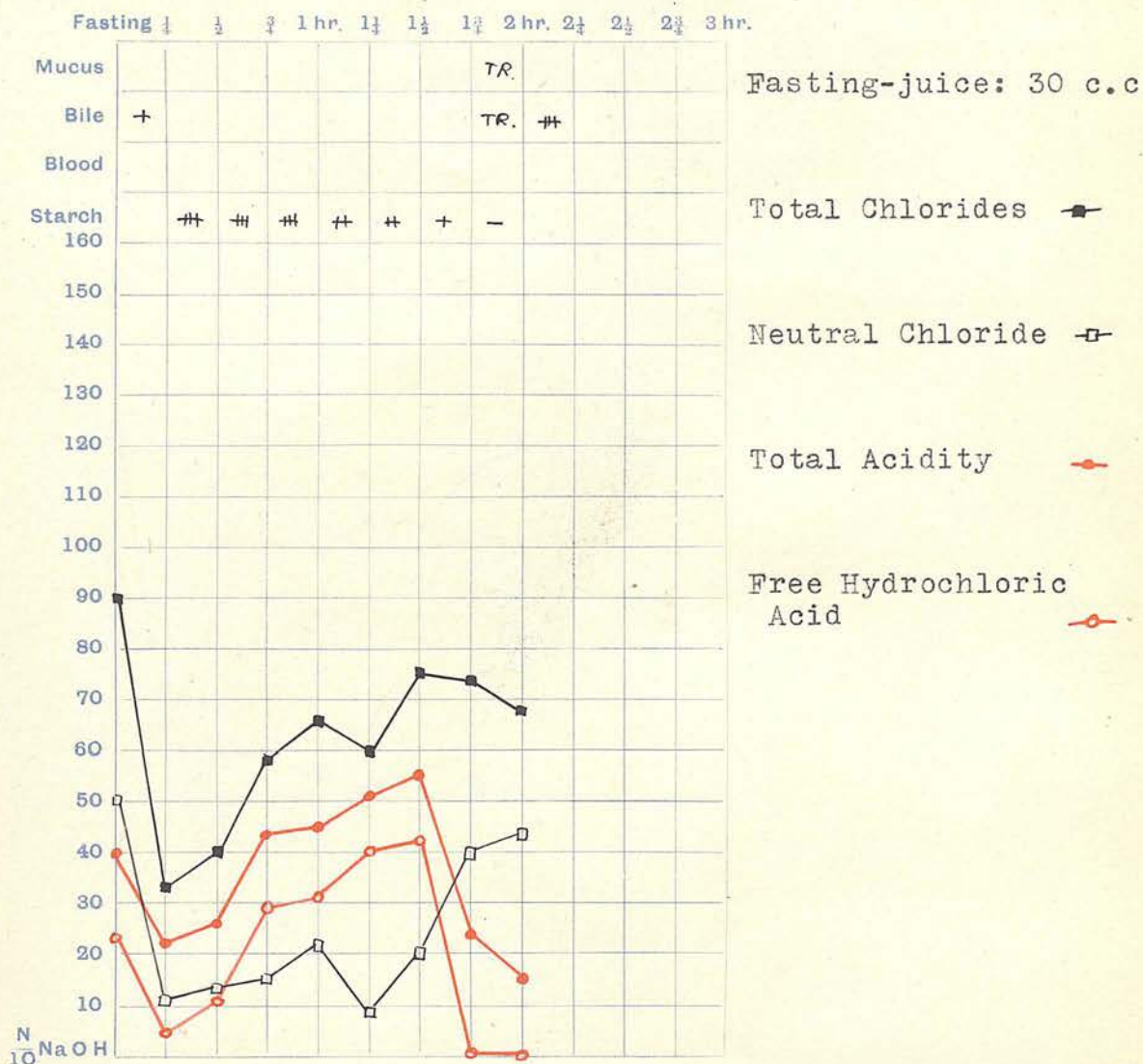
1. FRACTIONAL TEST-MEAL. Date 29. 6. '28.



Chronic duodenal ulcer (non-operated).

Name of Patient UD 10. (M. aet. 47)

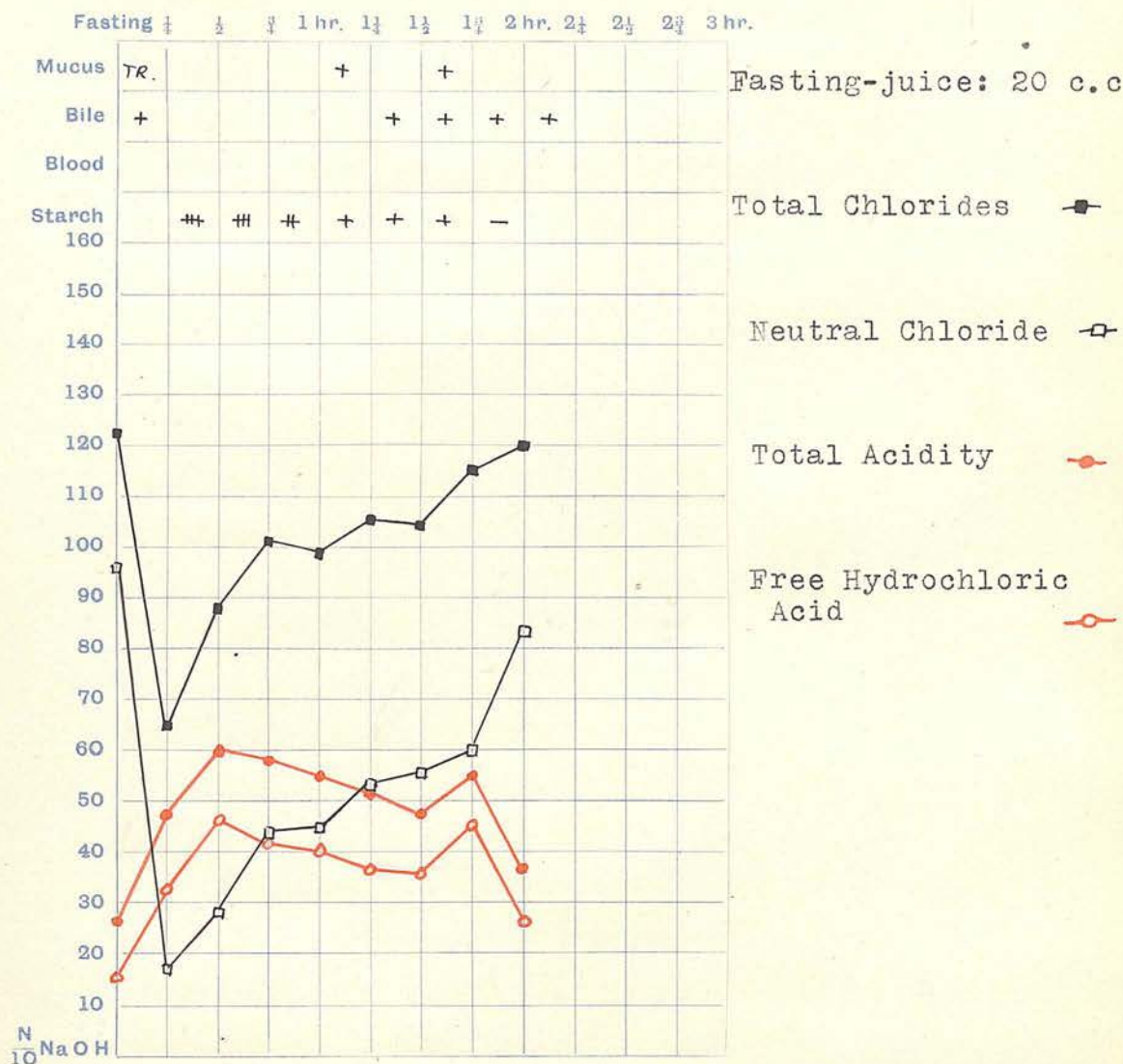
1. FRACTIONAL TEST-MEAL. Date 30. 7. '28.



Chronic duodenal ulcer (non-operated).

Name of Patient UD 11. (M. aet. 45)

1. FRACTIONAL TEST-MEAL. Date 20. 6. '29.

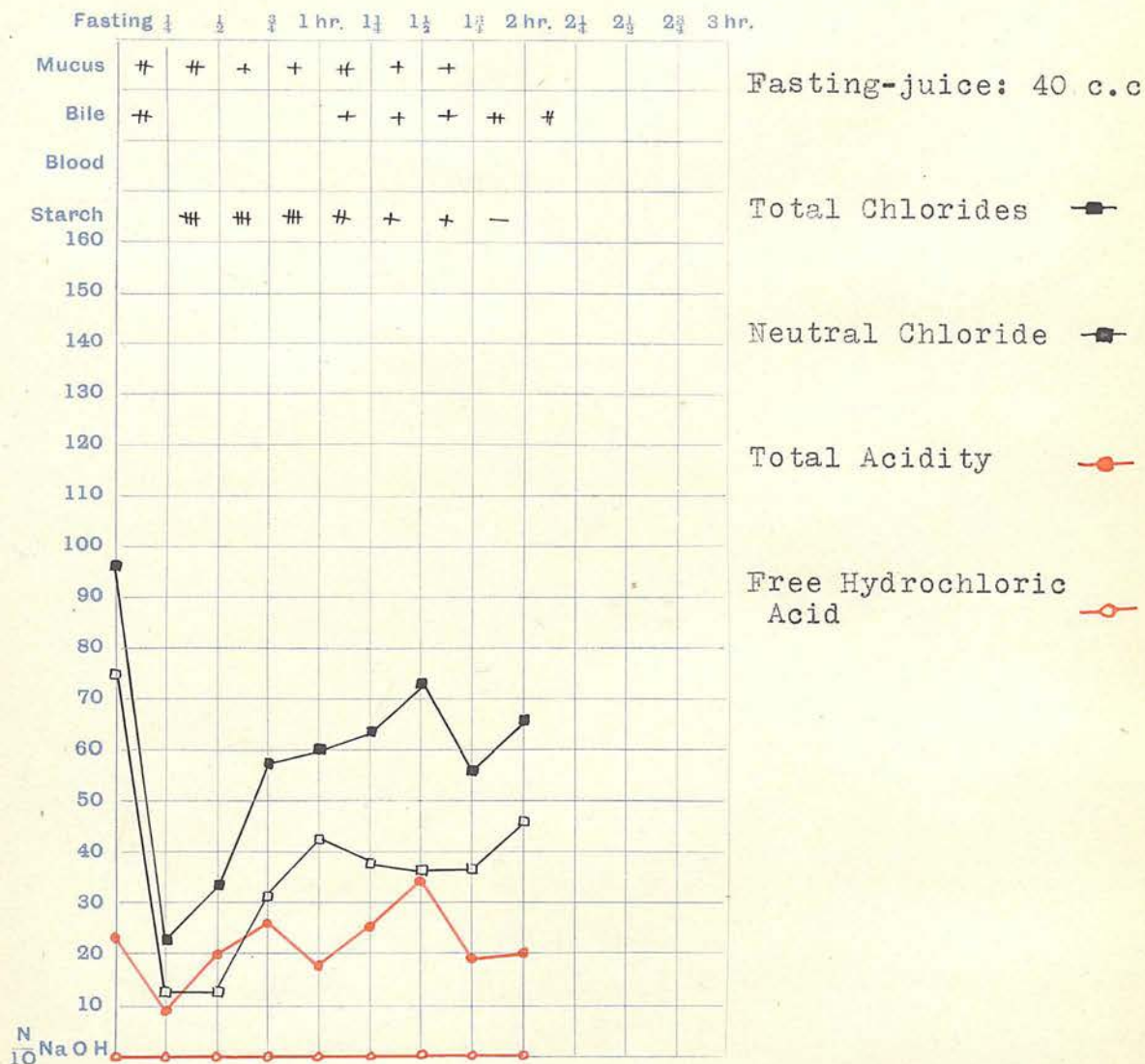


Chronic duodenal ulcer (non-operated).

Name of Patient VC 1. (F. aet. 24)

1. FRACTIONAL TEST-MEAL.

Date 16. 5. '28.

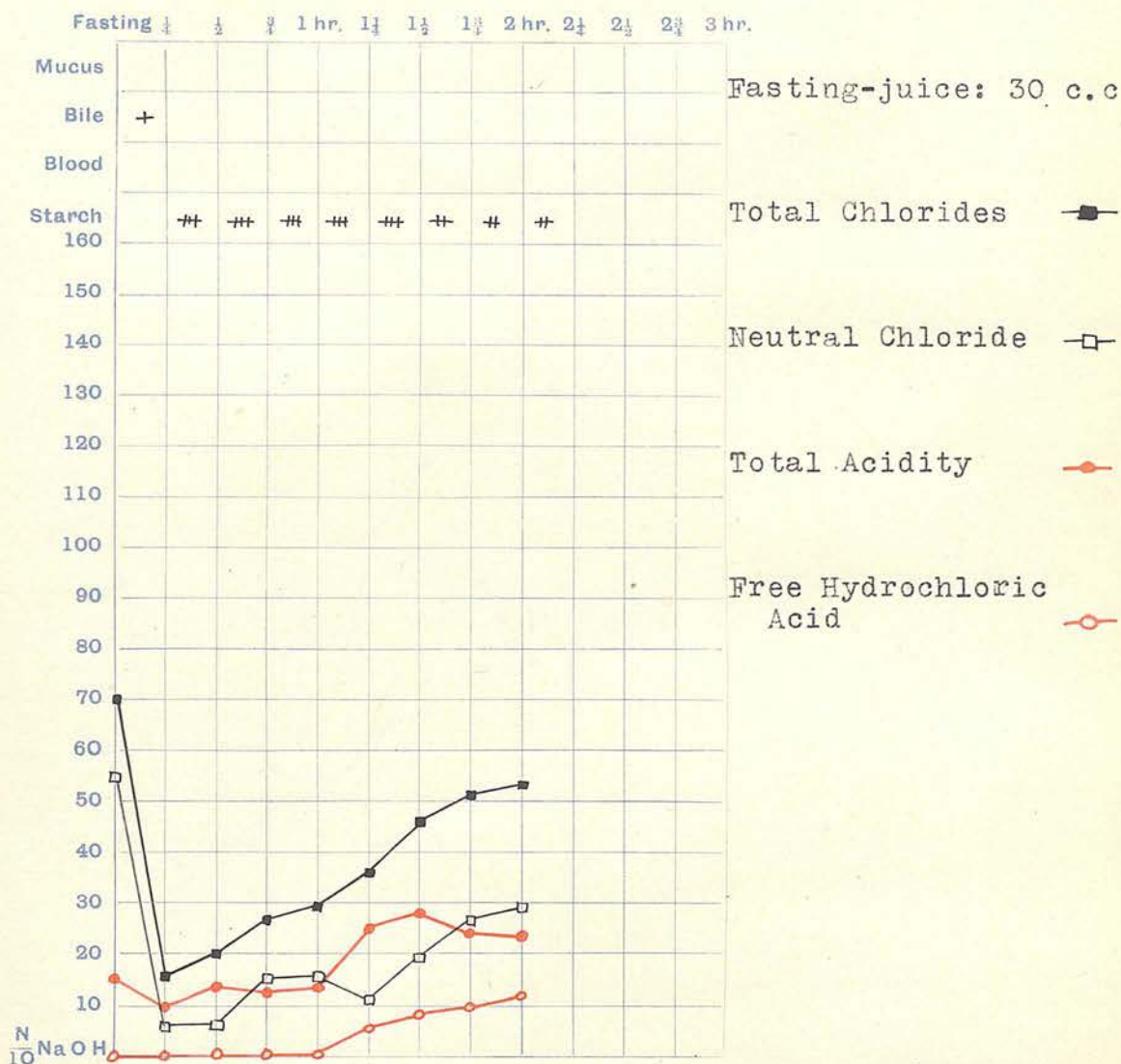


Cholelithiasis.

Name of Patient VC 2. (F. aet. 45)

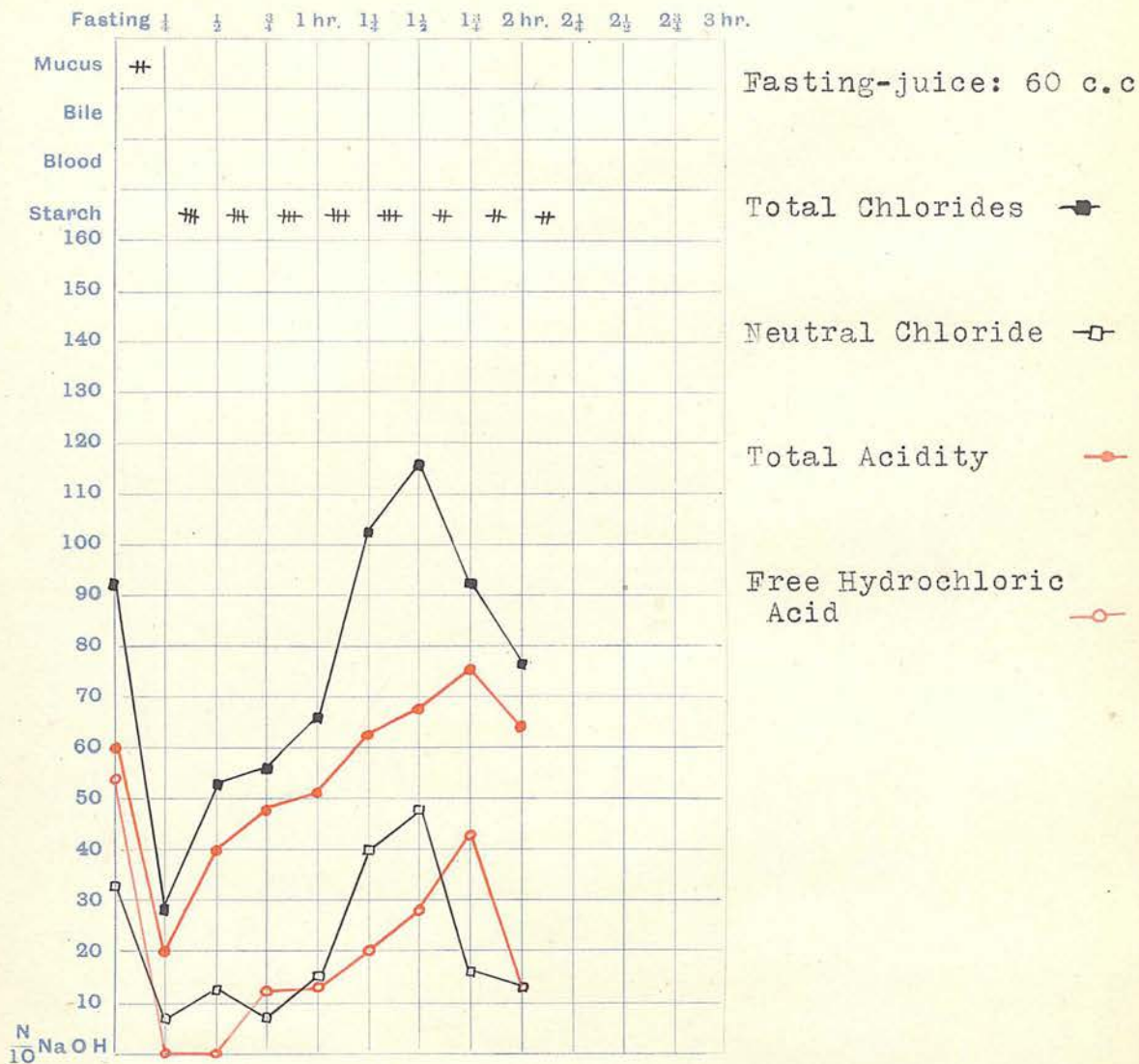
1. FRACTIONAL TEST-MEAL.

Date 3. 8. '28.



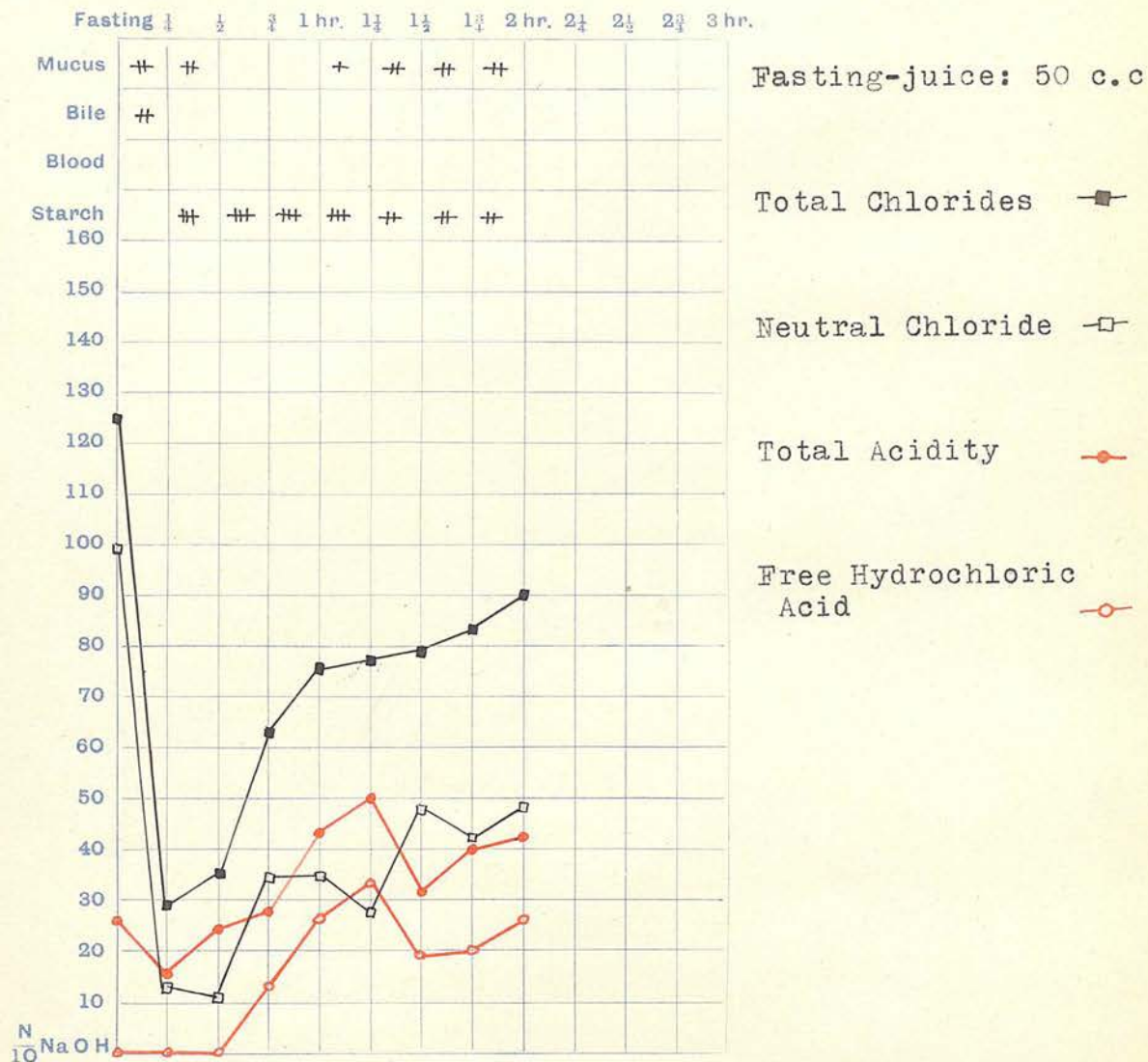
Cholelithiasis.

1. FRACTIONAL TEST-MEAL. Date 19. 4. '28.



Cholelithiasis.

1. FRACTIONAL TEST-MEAL. Date 7. 6. '28.

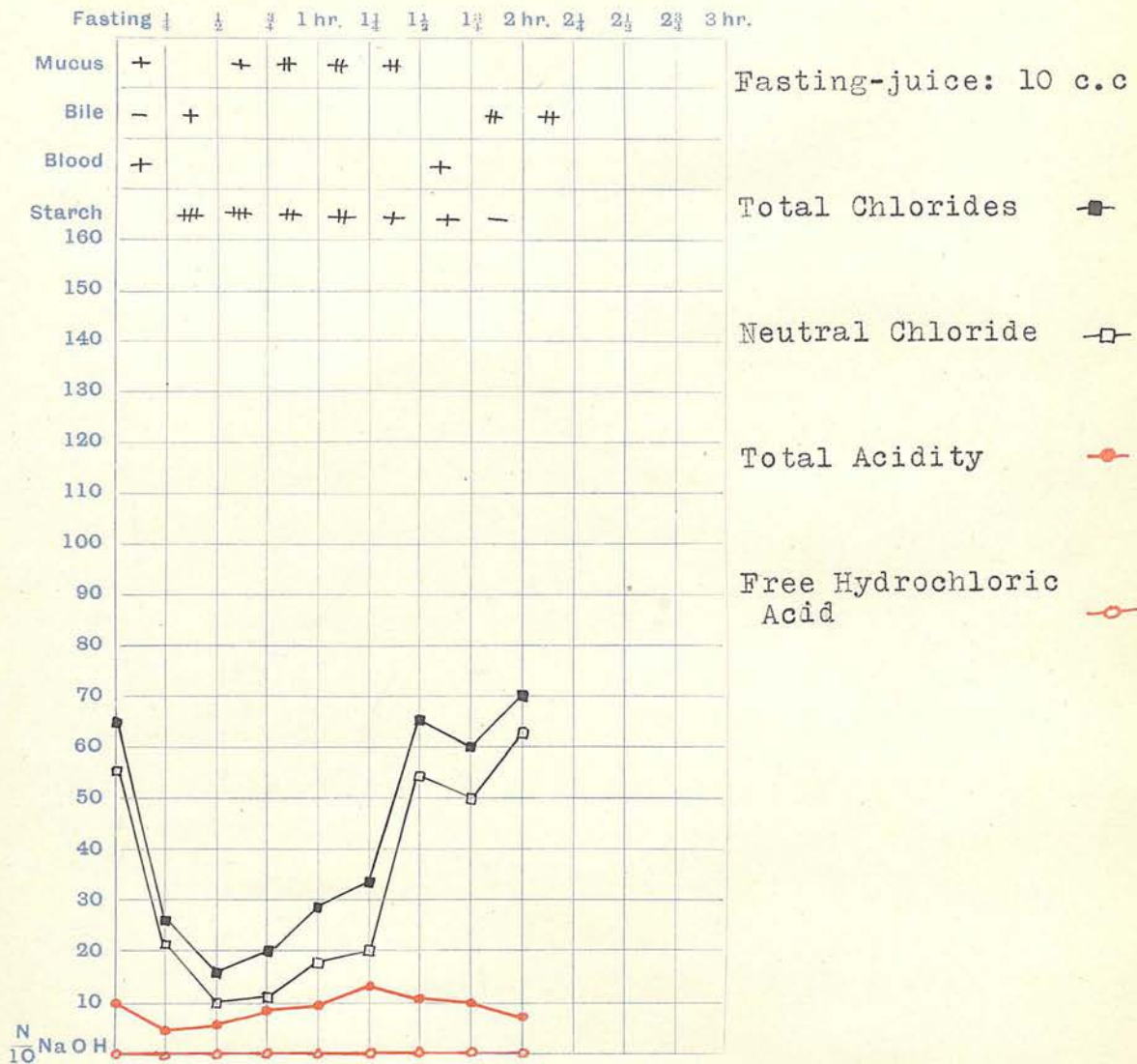


Cholelithiasis.

Name of Patient VC 5. (F. aet. 50)

1. FRACTIONAL TEST-MEAL.

Date 30. 5. '28.

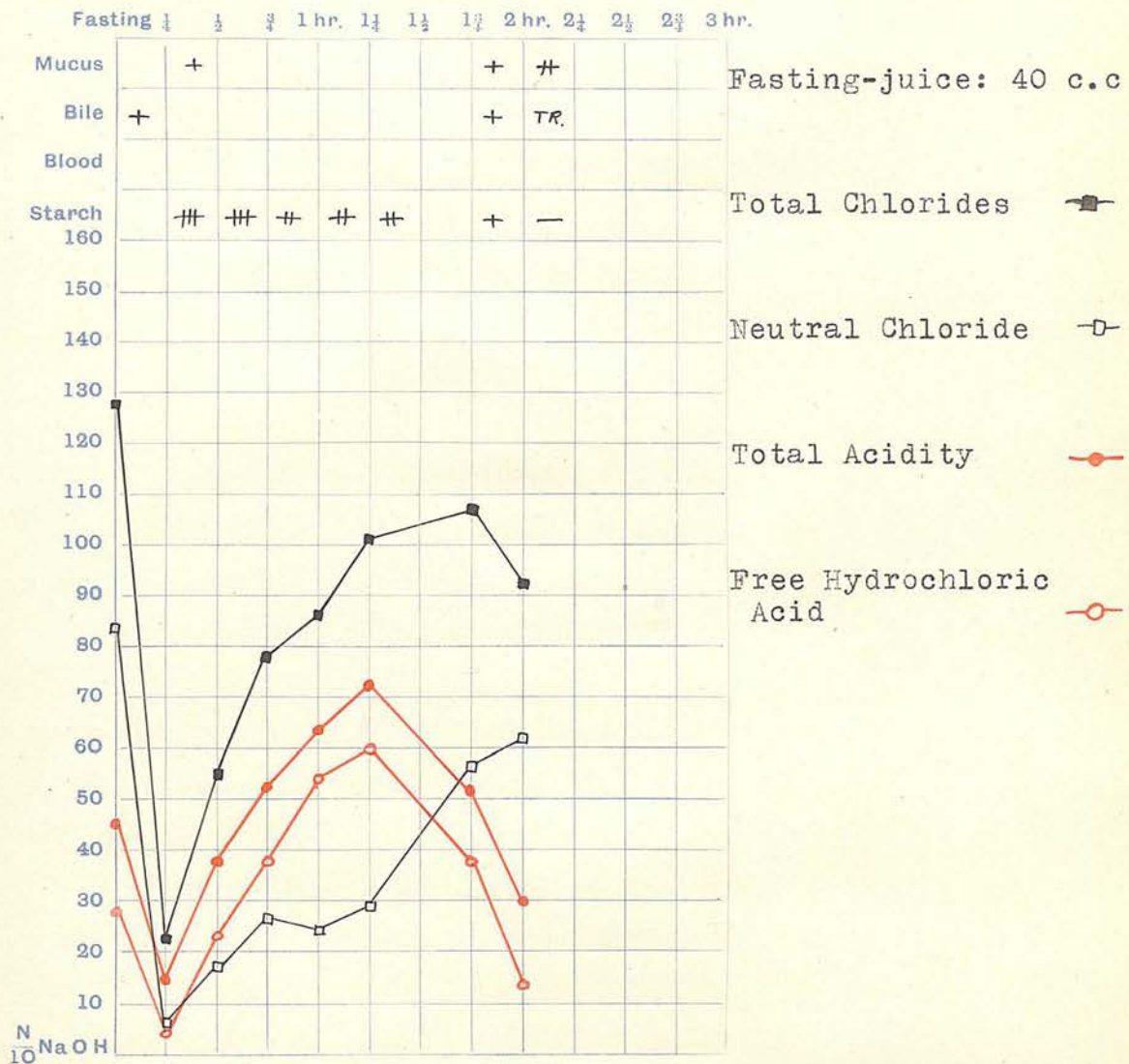


Cholelithiasis.

Name of Patient VC 6. (M. aet. 46)

1. FRACTIONAL TEST-MEAL.

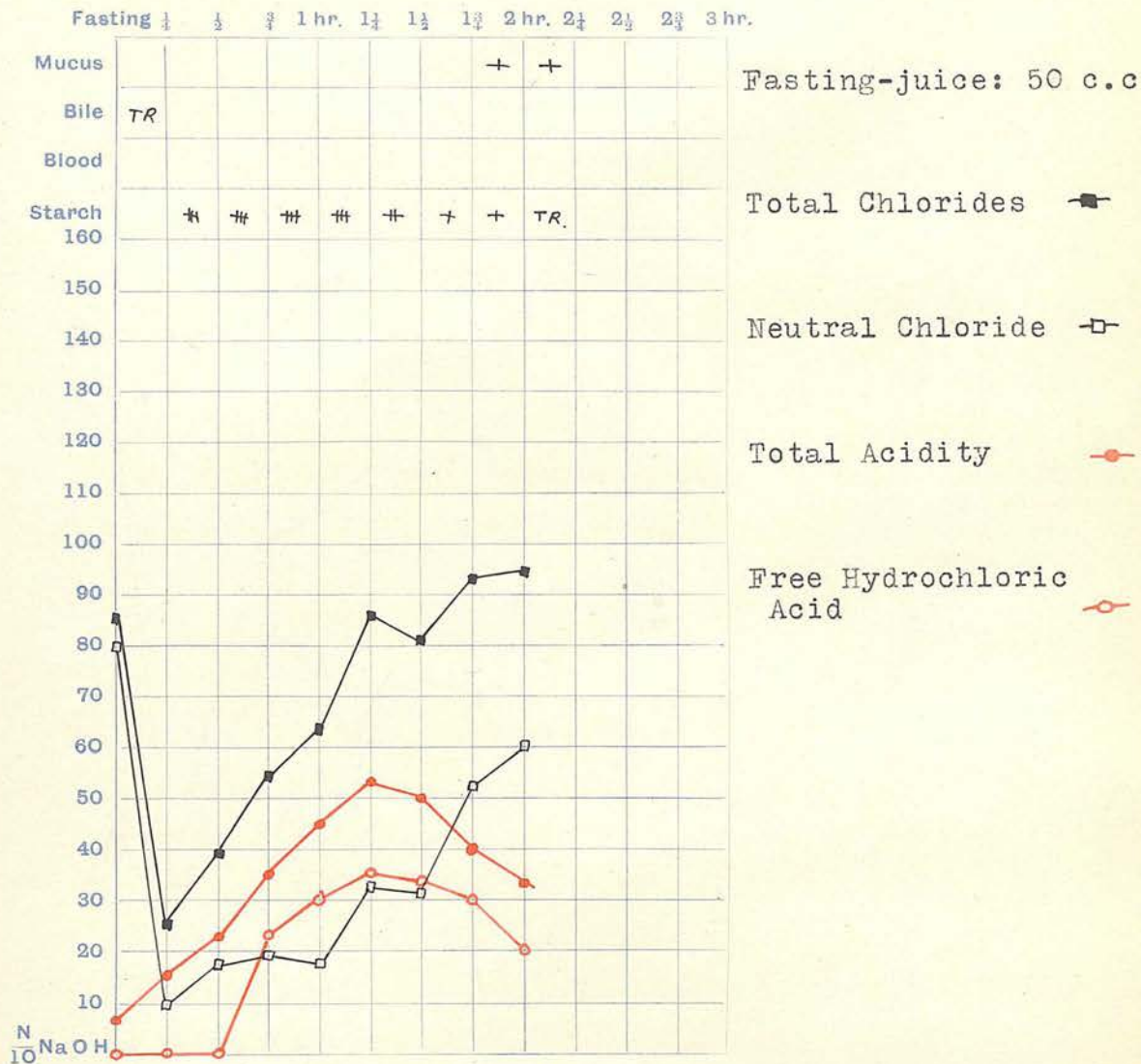
Date 28. 5. '28.



Cholelithiasis.

Name of Patient AV 1. (F. aet. 29)

1. FRACTIONAL TEST-MEAL. Date 7. 3. '29.

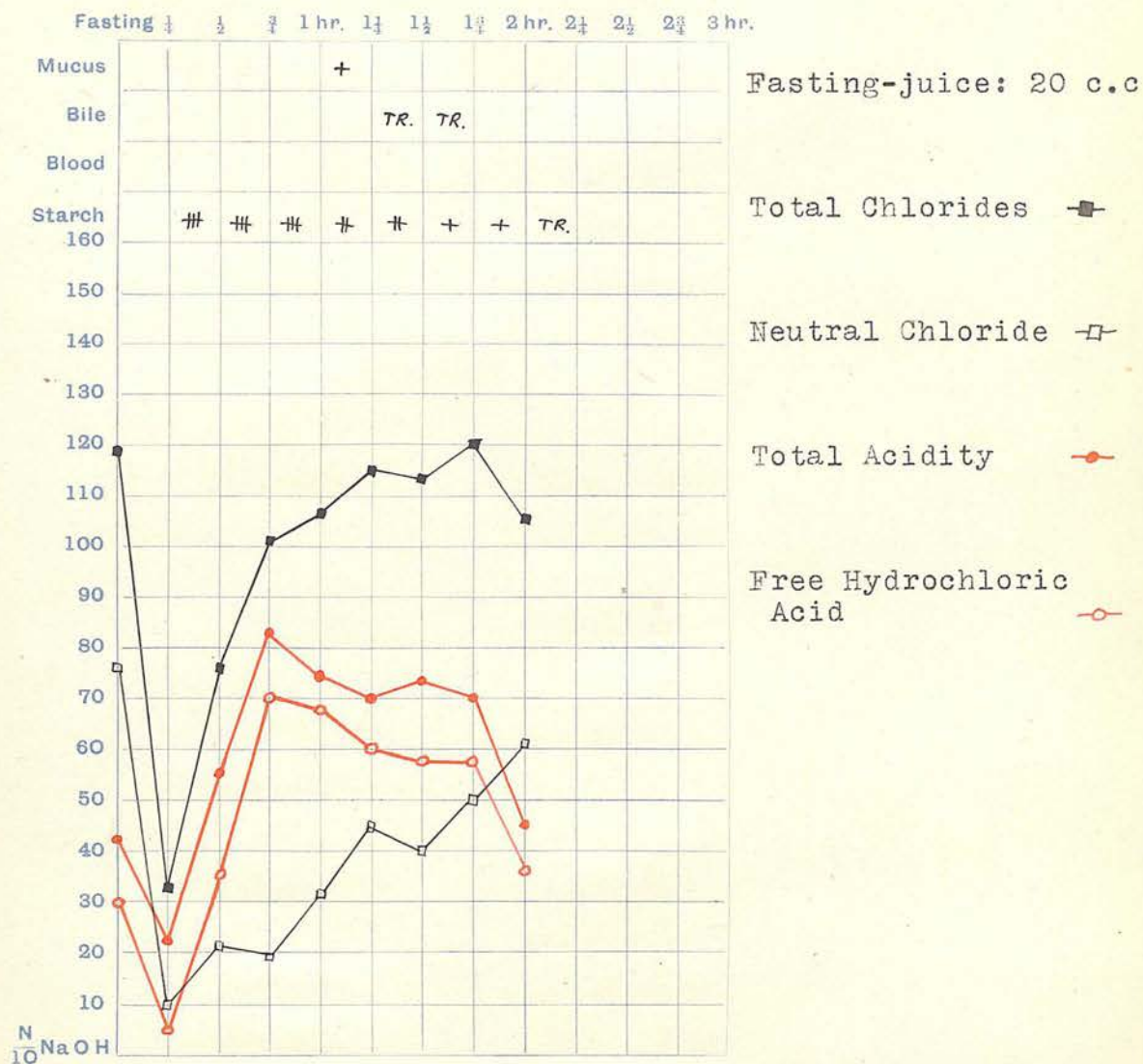


Chronic appendicitis.

Name of Patient AV 2. (M. aet. 38)

1. FRACTIONAL TEST-MEAL.

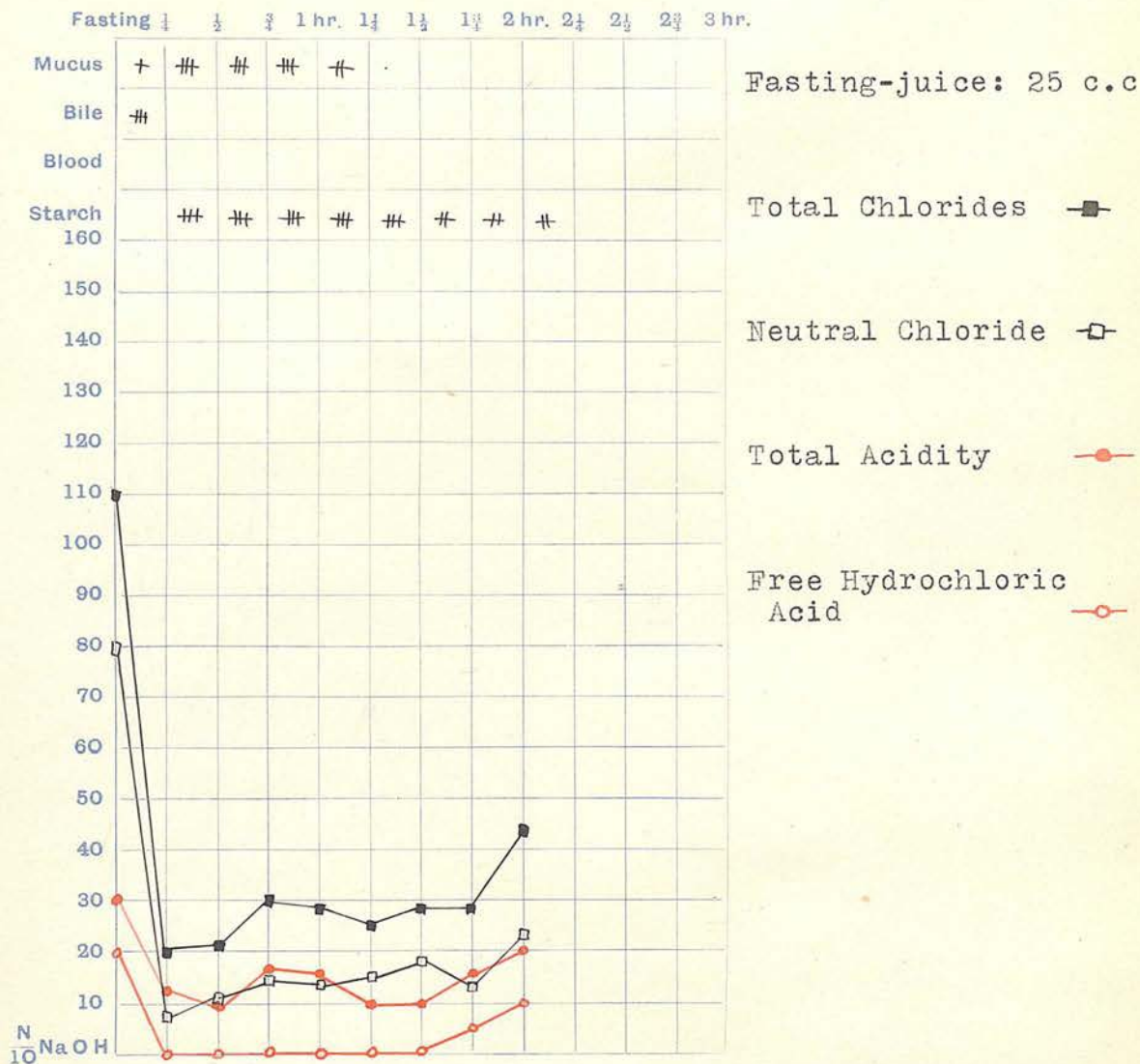
Date 27. 3. '29.



Chronic appendicitis.

Name of Patient AV 3. (F. aet. 28)

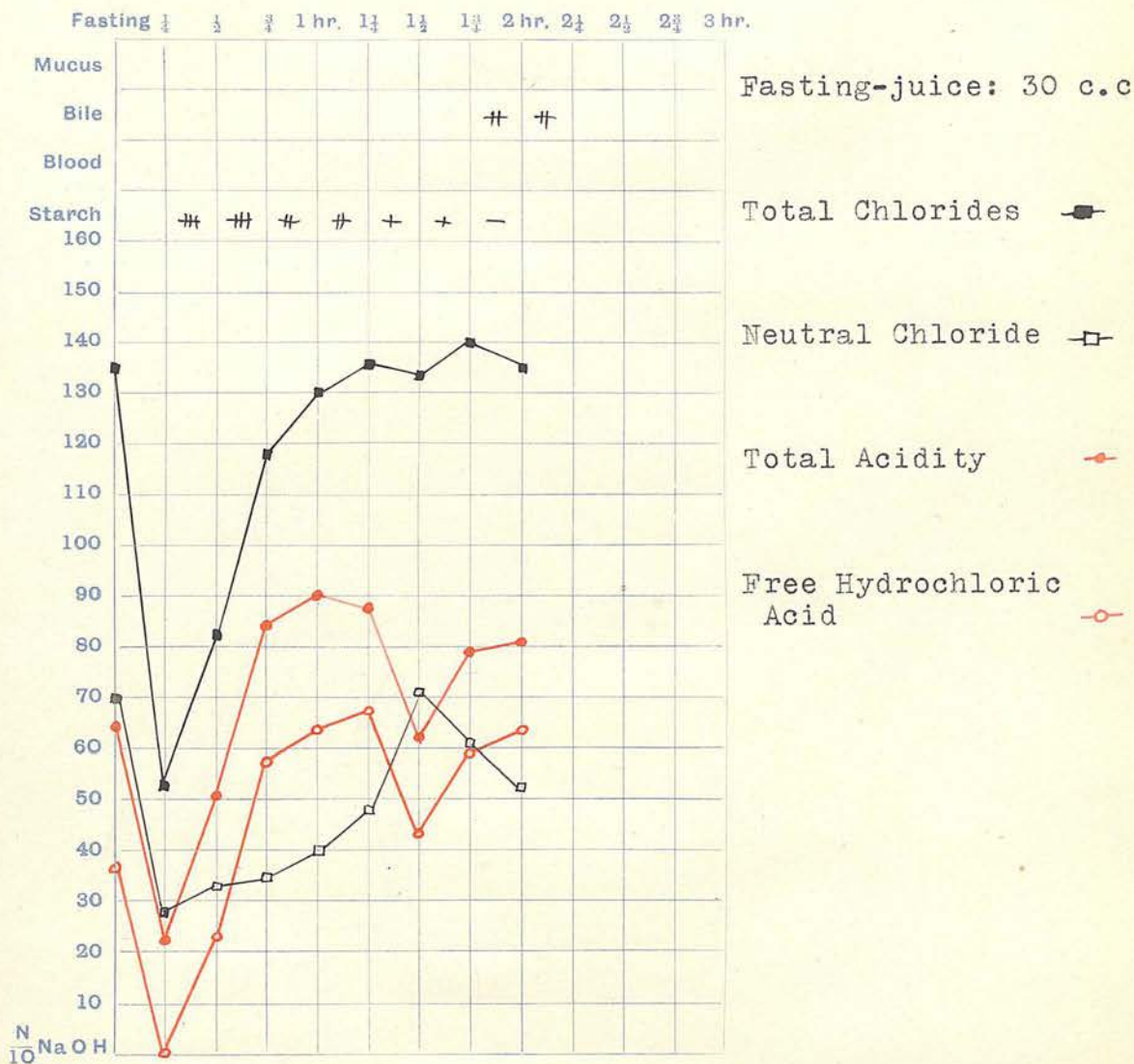
1. FRACTIONAL TEST-MEAL. Date 29. 12. '28.



Chronic appendicitis.

Name of Patient AV 4.(A) (M. aet. 26)

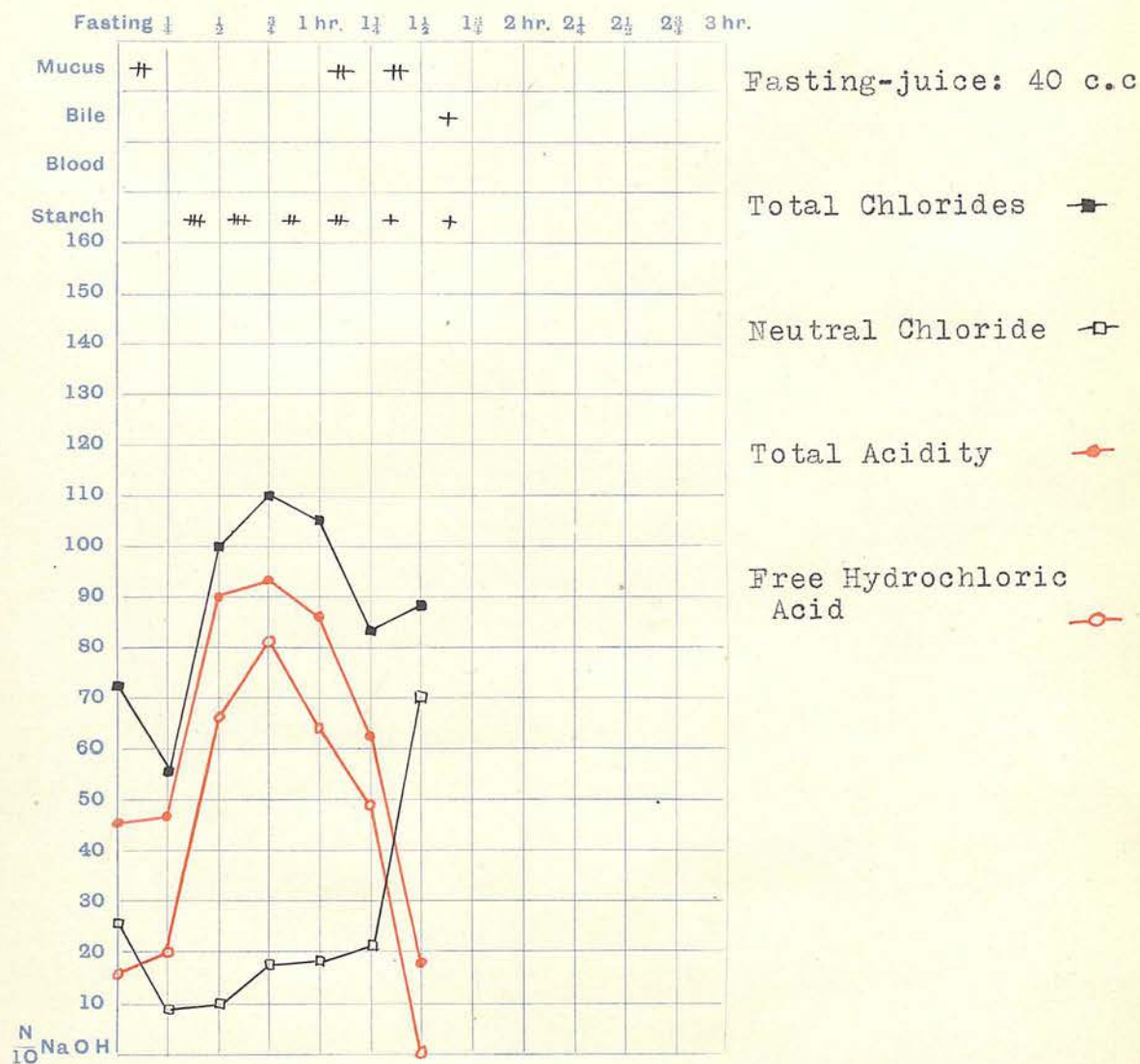
1. FRACTIONAL TEST-MEAL. Date 29. 4. '28.



Chronic appendicitis, preoperative.

Name of Patient AV 4.(B) (M. aet. 26)

1. FRACTIONAL TEST-MEAL. Date 10. 5. '28.

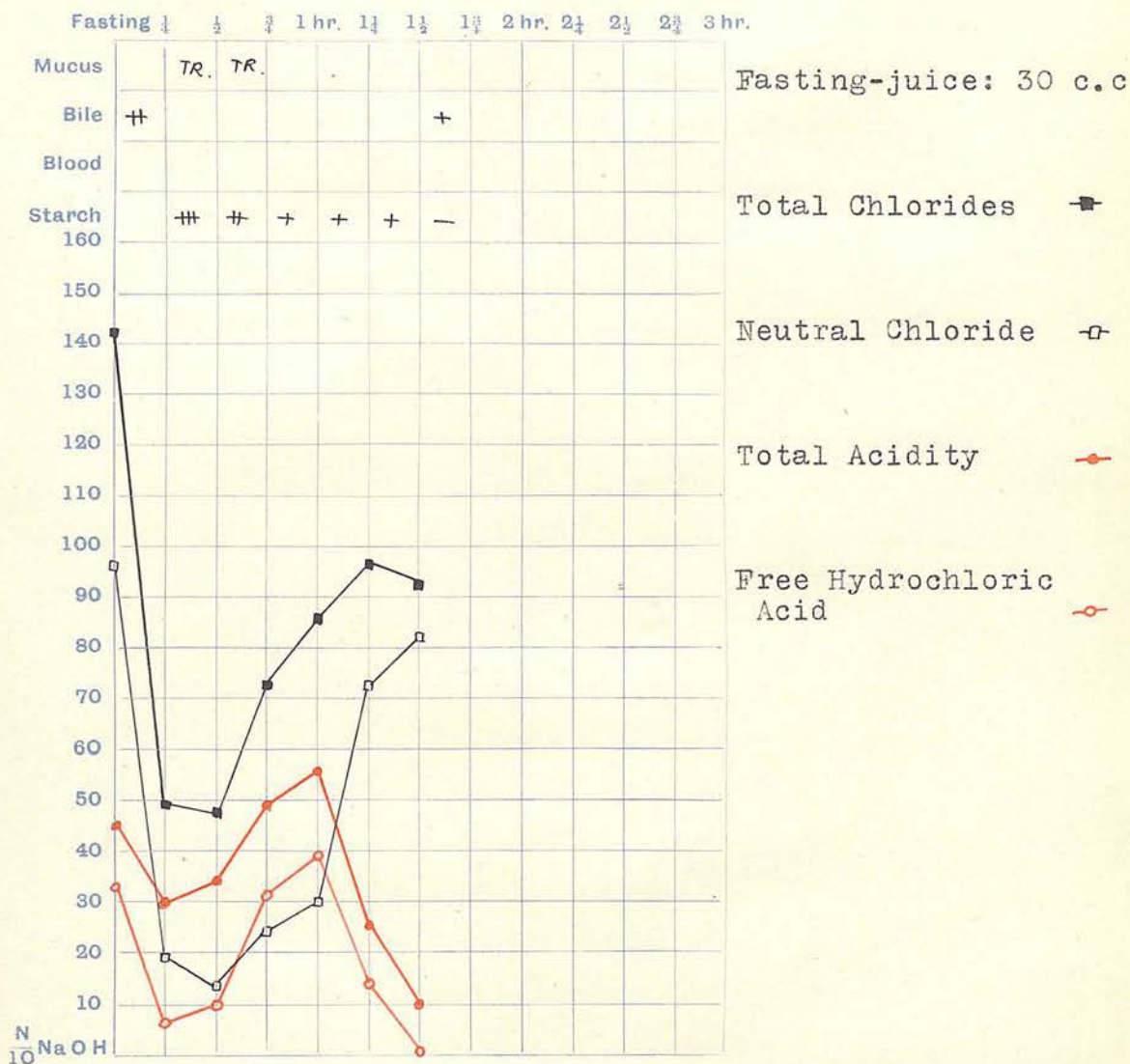


Ten days after appendicectomy.

Name of Patient AV 5. (M. aet. 34)

1. FRACTIONAL TEST-MEAL.

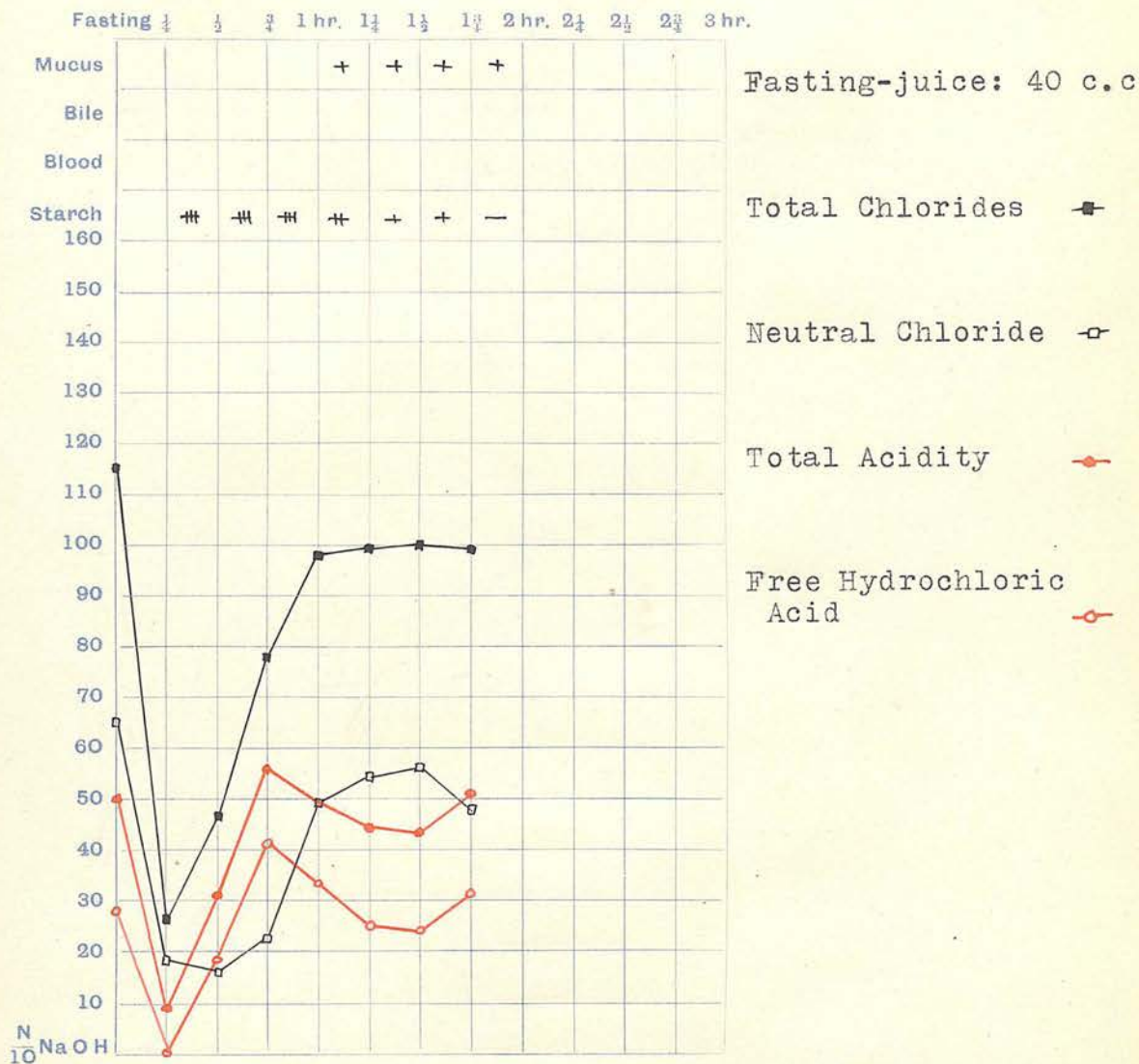
Date 20. 6. '28.



Chronic appendicitis.

Name of Patient AV 6. (M. aet. 25)

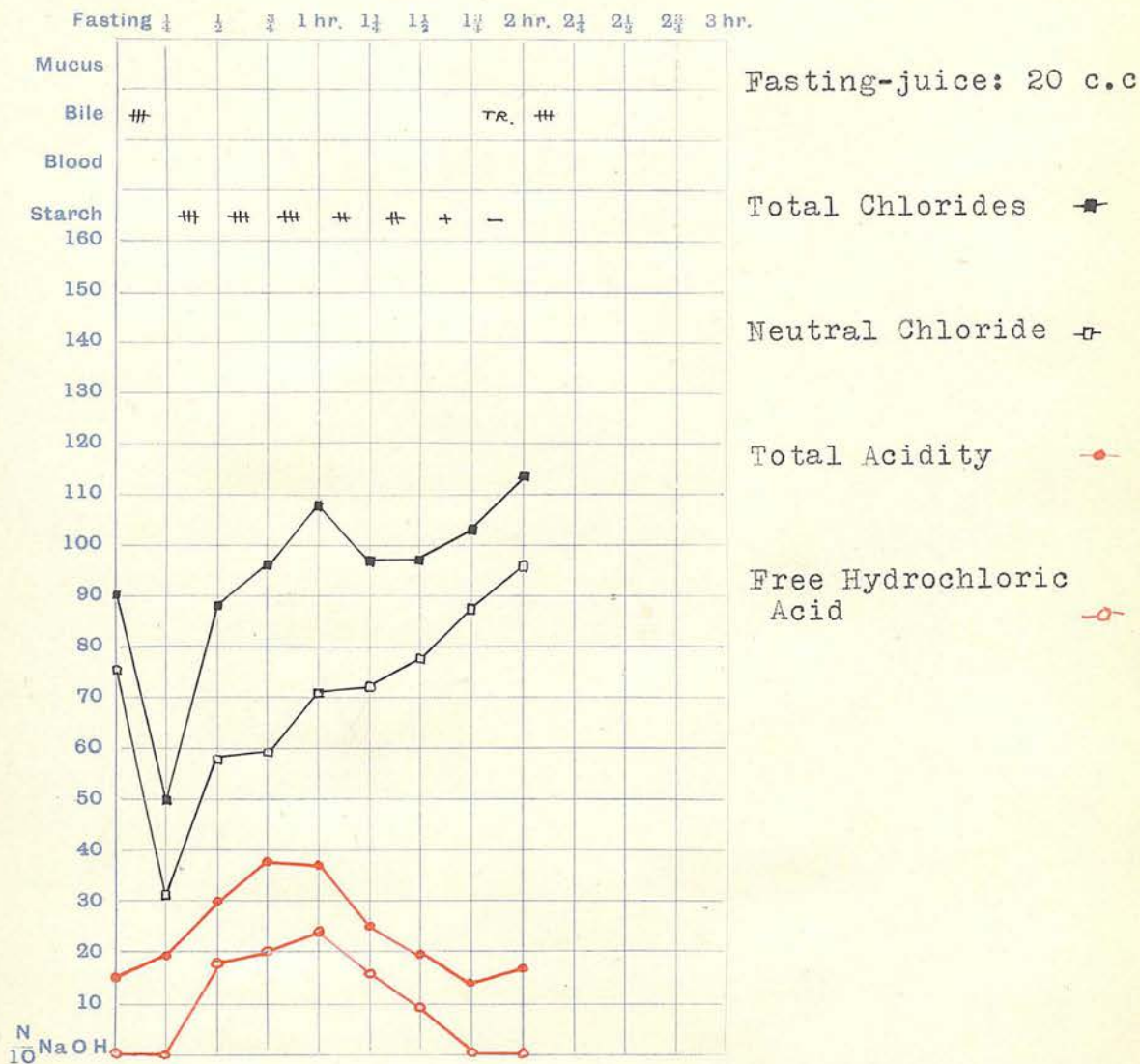
1. FRACTIONAL TEST-MEAL. Date 13. 7. '28.



Chronic appendicitis.

Name of Patient AV 7. (F. aet. 26)

1. FRACTIONAL TEST-MEAL. Date 22. 6. '29.



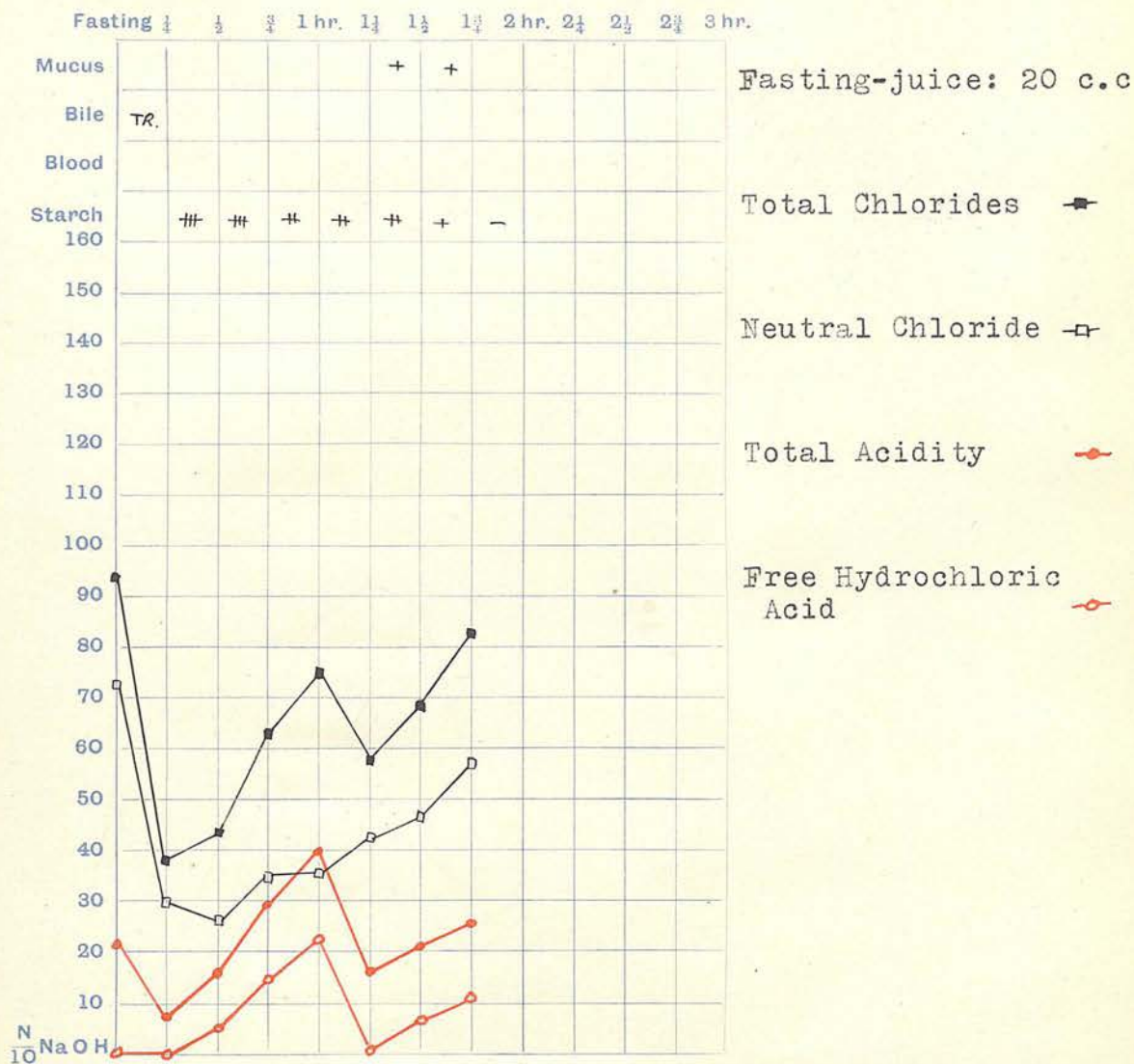
Chronic appendicitis.

Name of Patient AV 8.

(M. aet. 31)

1. FRACTIONAL TEST-MEAL.

Date 29. 7. '29.

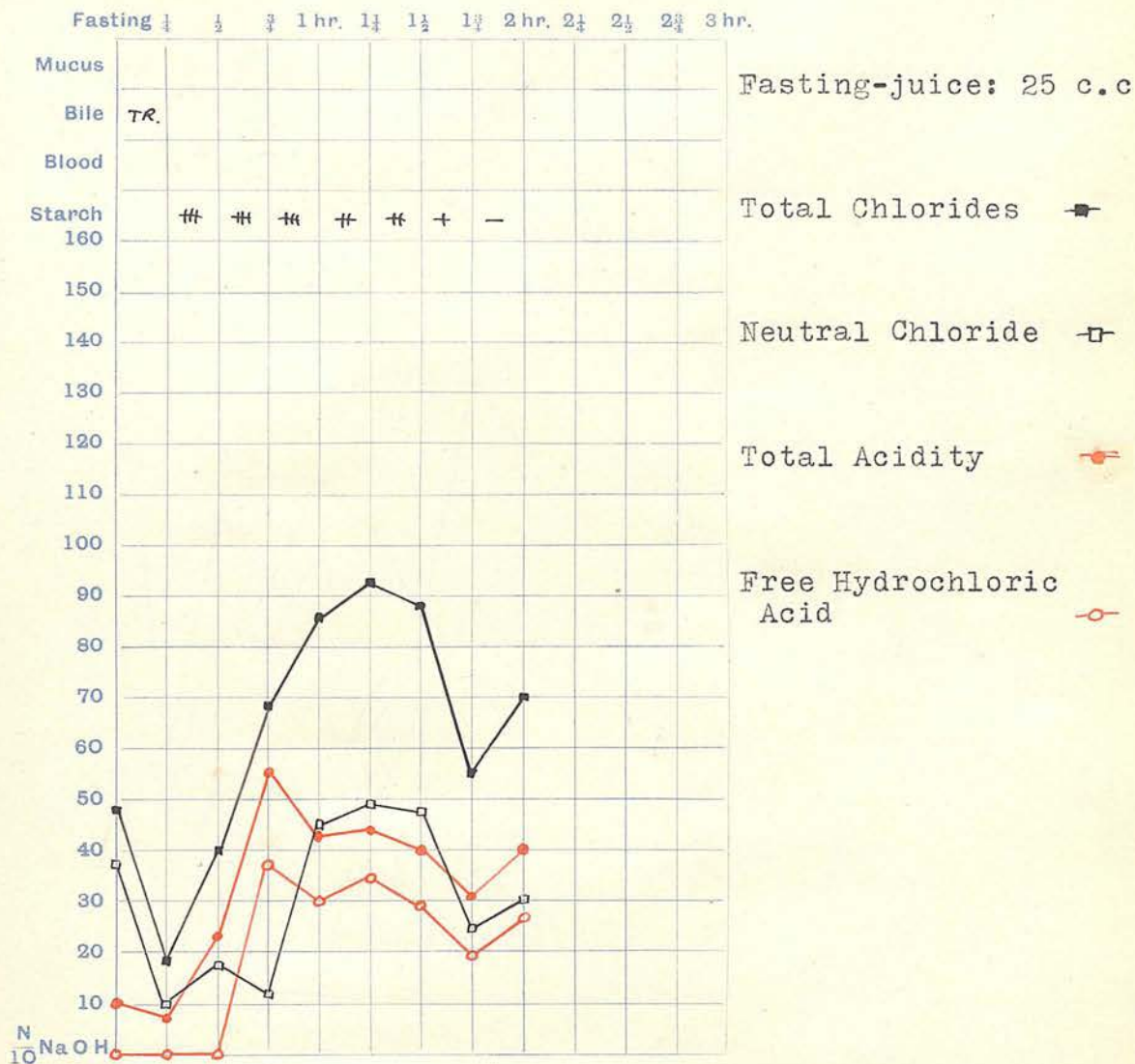


Chronic appendicitis.

Name of Patient AV 9. (M. aet. 30)

1. FRACTIONAL TEST-MEAL.

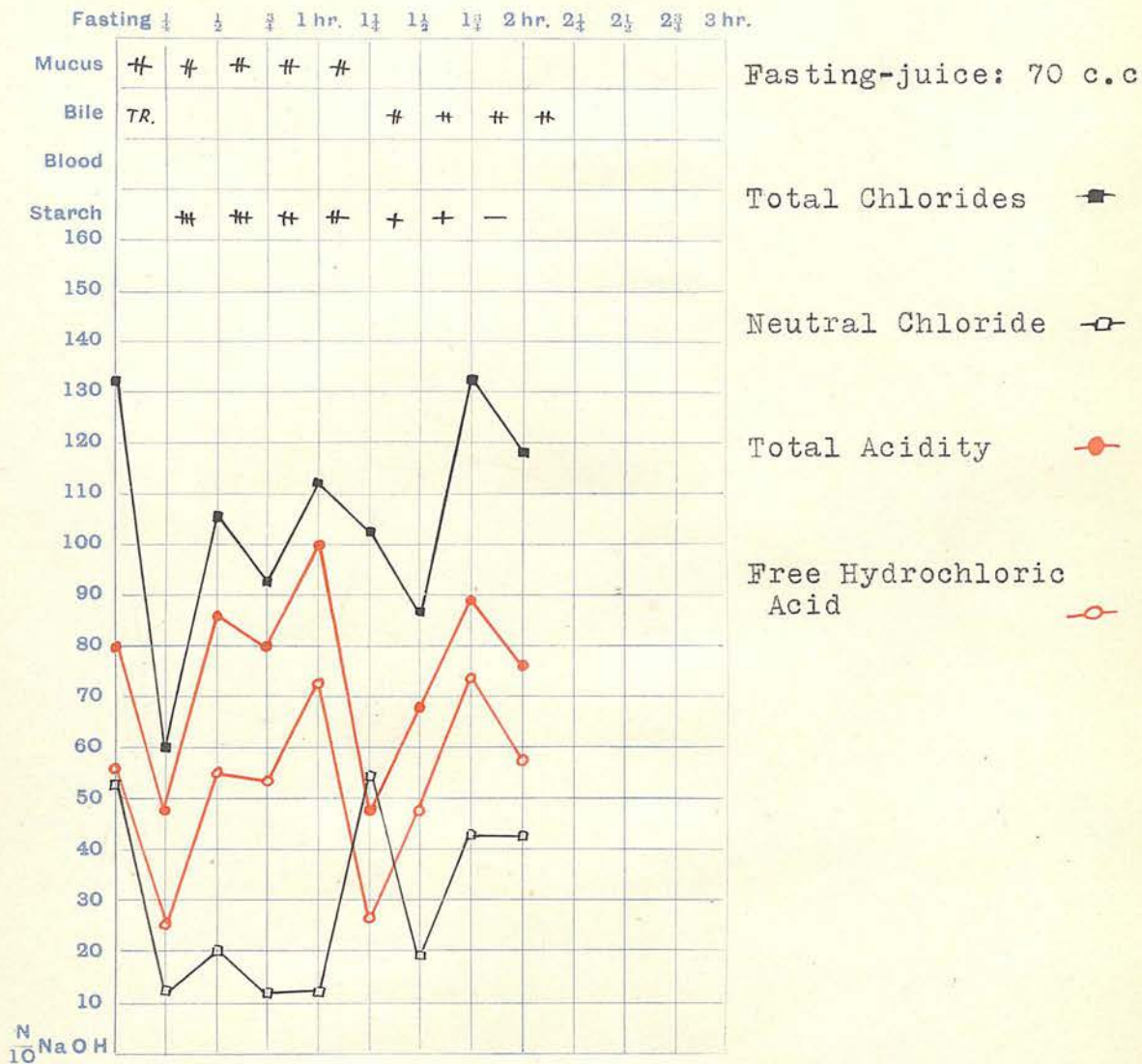
Date 11. 7. '28.



Chronic appendicitis.

Name of Patient AV 10. (M. aet. 25)

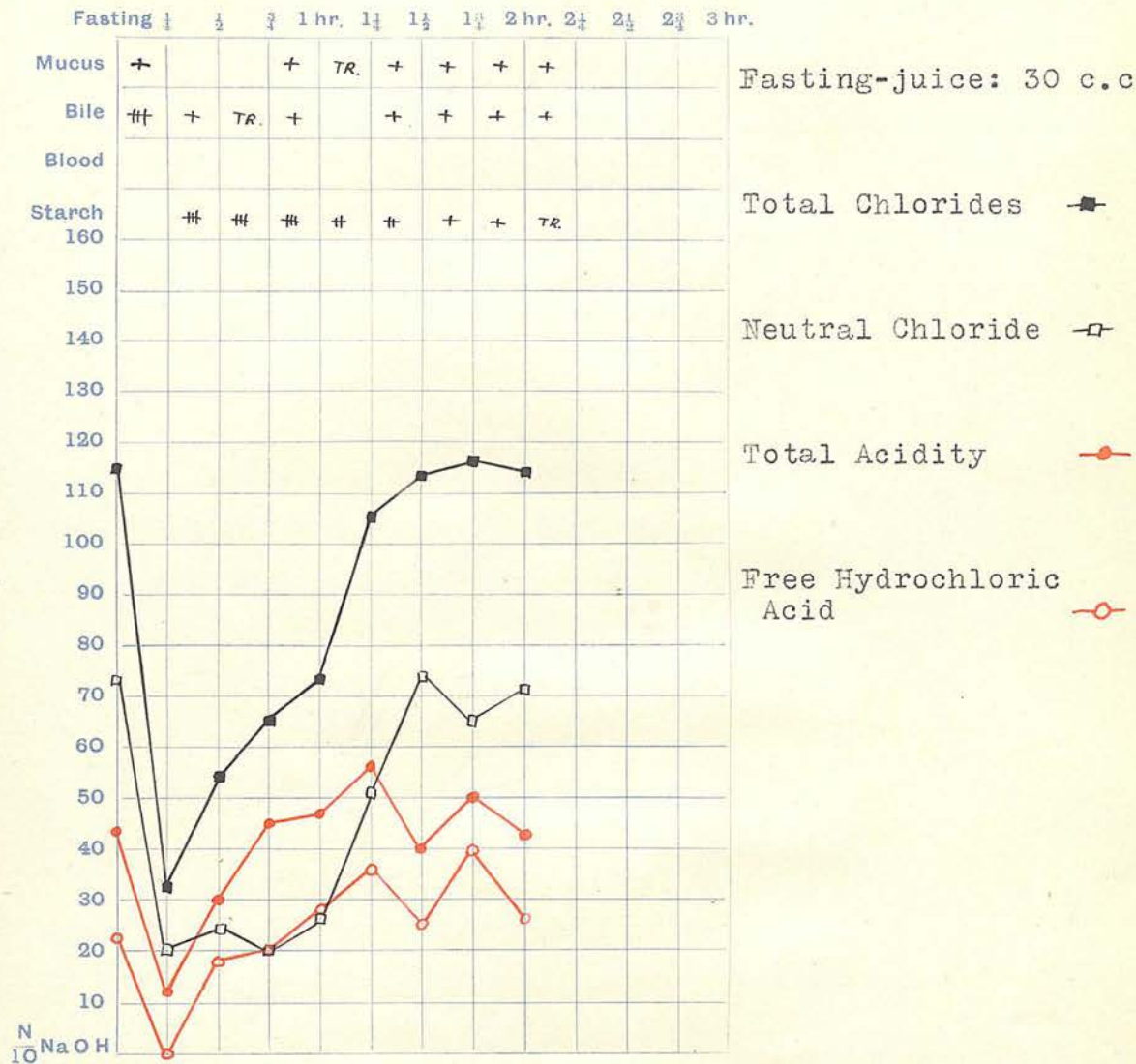
1. FRACTIONAL TEST-MEAL. Date 22. 4. '28.



Chronic appendicitis, non-operated.

Name of Patient AV 11. (M. aet. 28)

1. FRACTIONAL TEST-MEAL. Date 13. 3. '29.

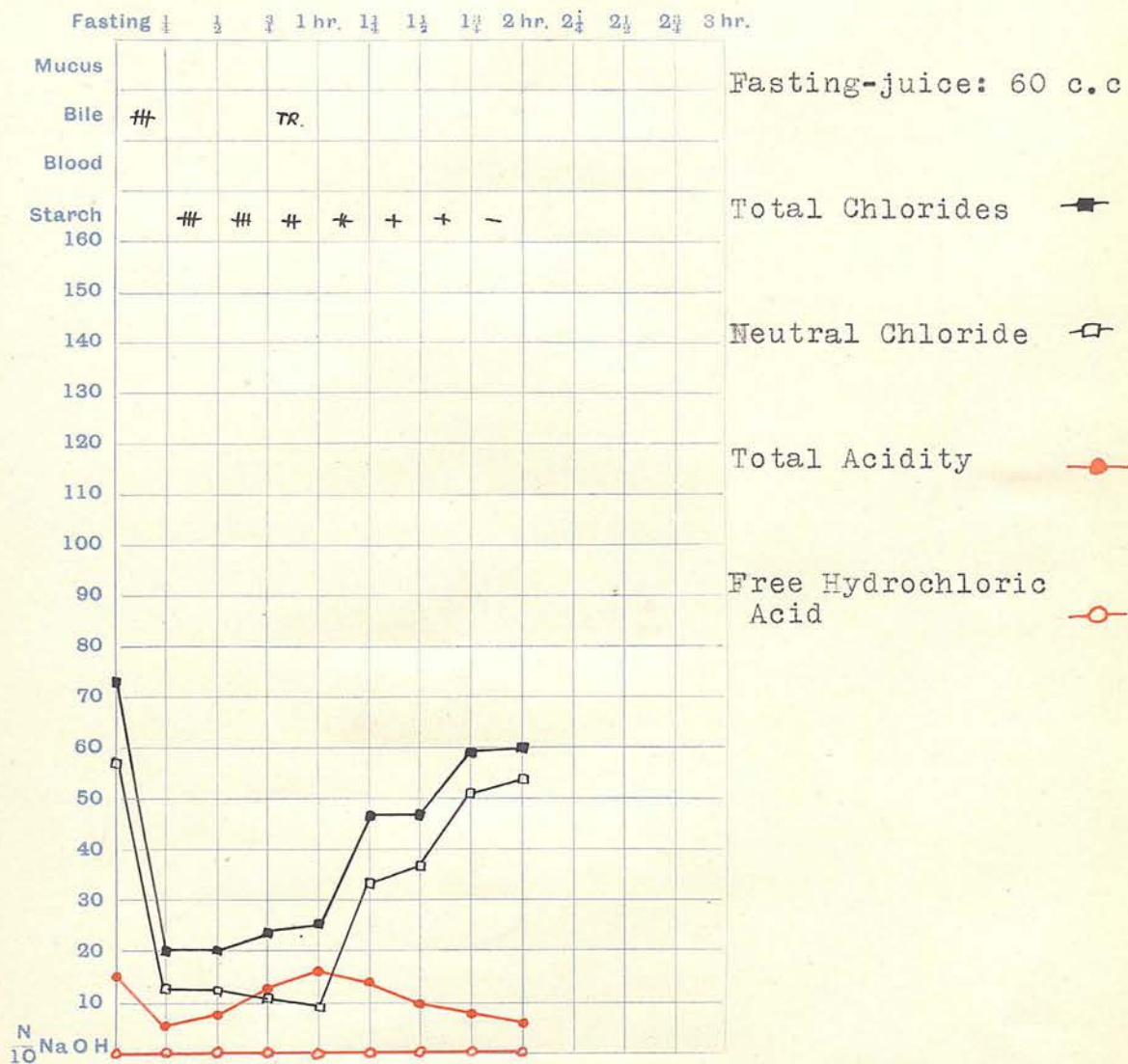


Chronic appendicitis, non-operated.

Name of Patient PA 1. (M. aet. 50)

1. FRACTIONAL TEST-MEAL.

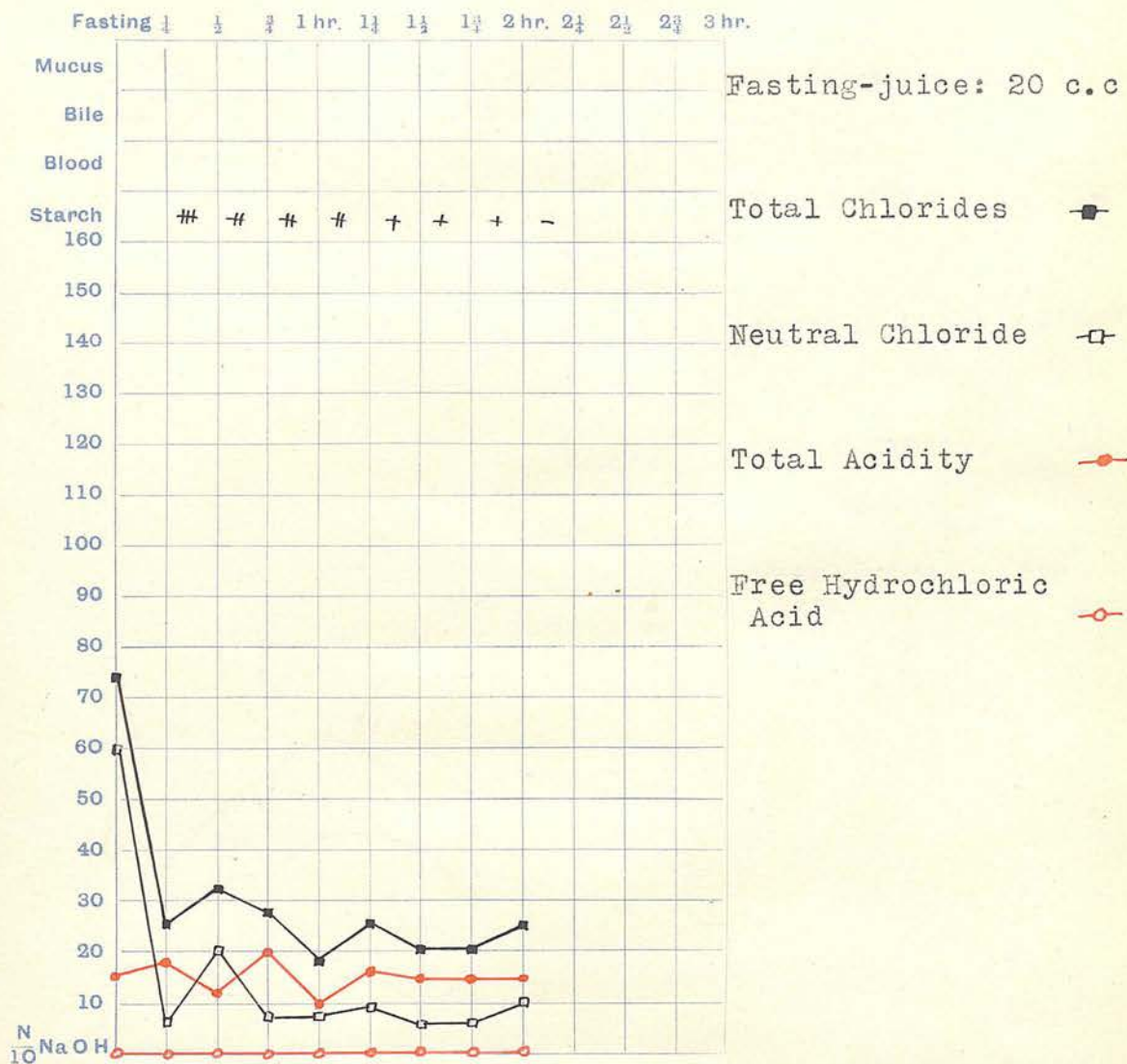
Date 26. 4. '29.



Pernicious anaemia.

1. FRACTIONAL TEST-MEAL.

Date 28. 3. '29.

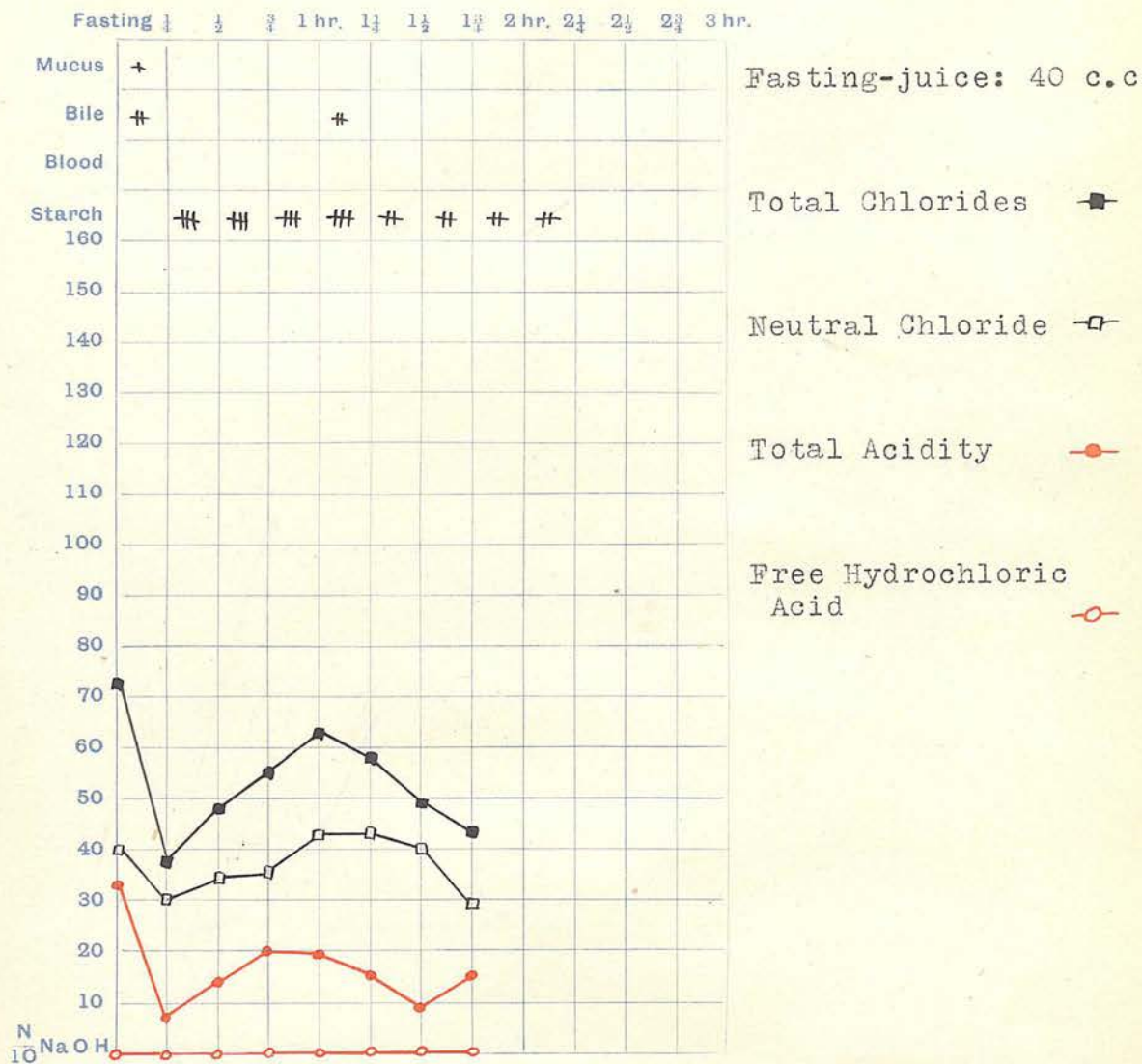


Pernicious anaemia.

Name of Patient PA 3. (F. aet. 48)

1. FRACTIONAL TEST-MEAL.

Date 2. 5. '28.

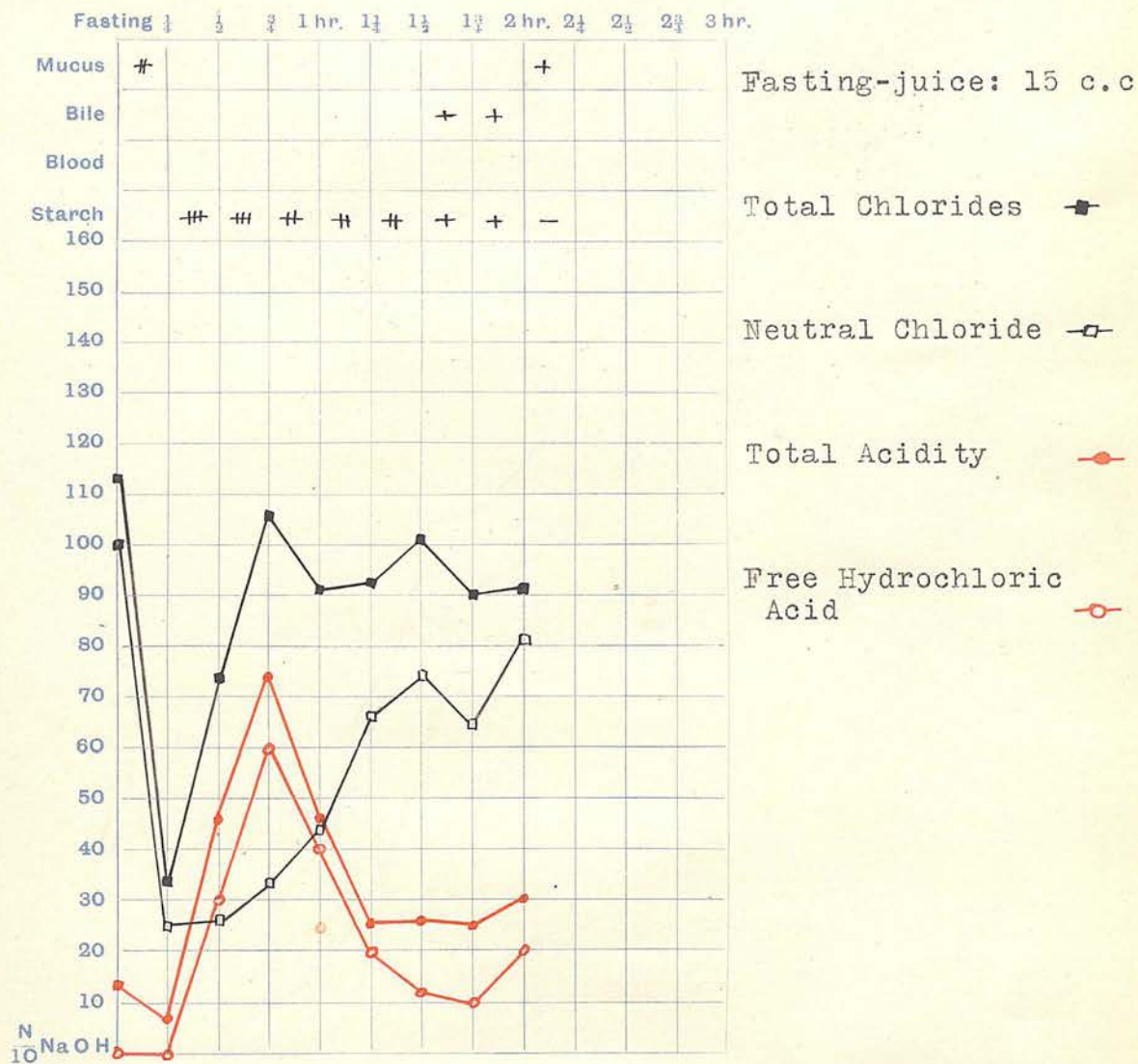


Pernicious anaemia.

Name of Patient F 1. (M. aet. 46)

1. FRACTIONAL TEST-MEAL.

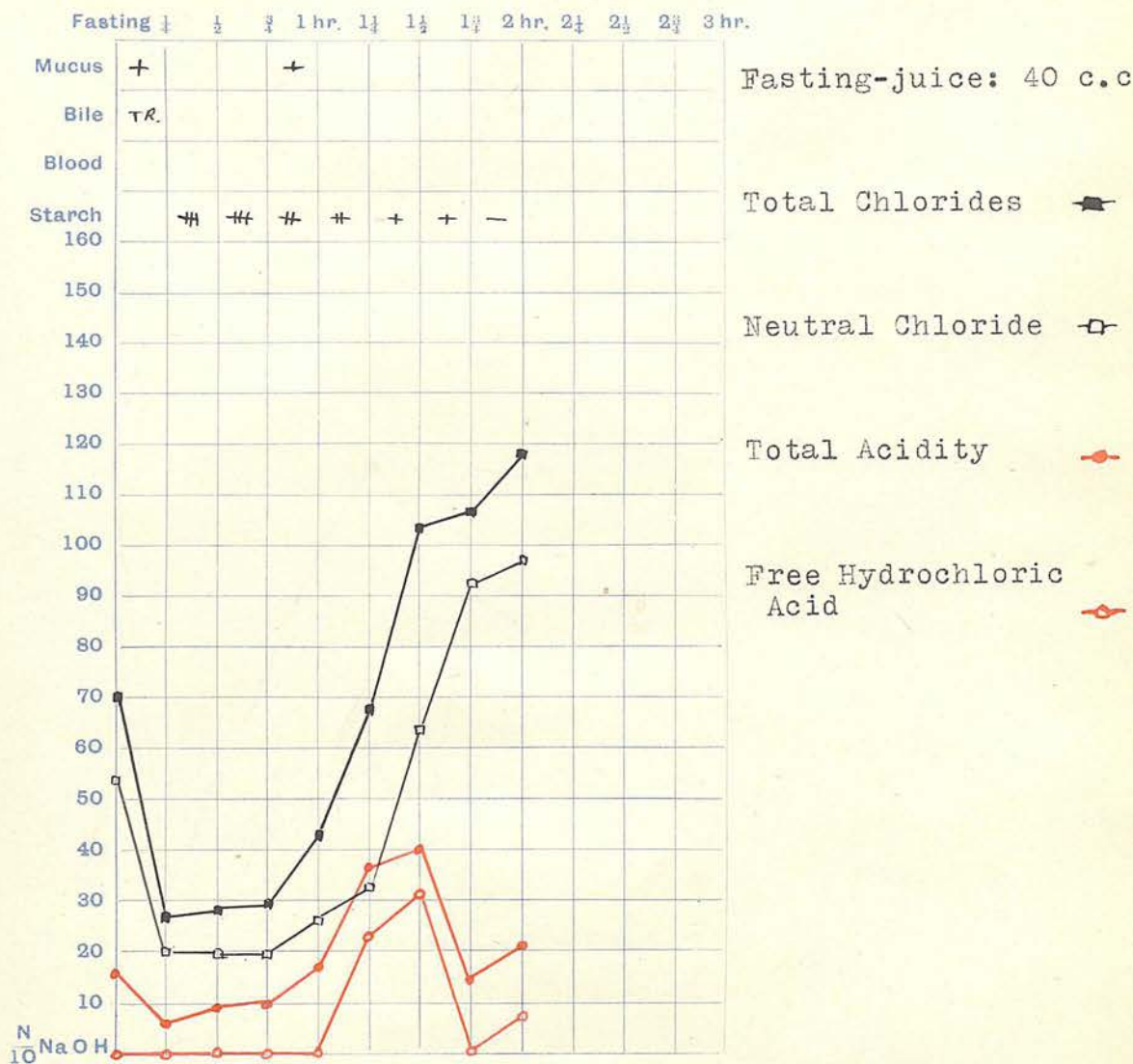
Date 27. 5. '29.



Nil definite found at operation.

Name of Patient F 2. (F. aet. 43)

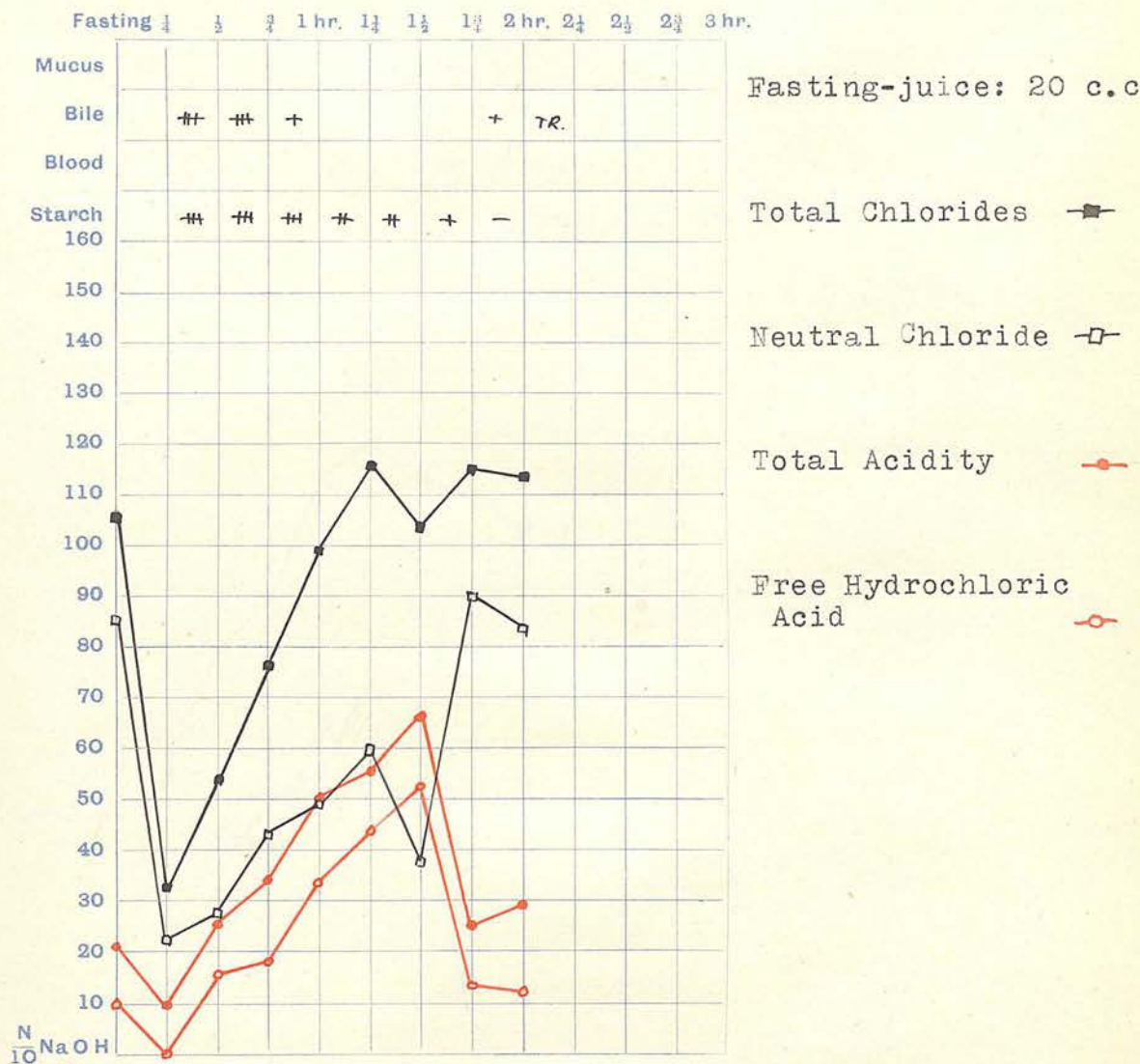
1. FRACTIONAL TEST-MEAL. Date 28. 5. '29.



Nil definite found at operation.

Name of Patient F 3. (F. aet. 56)

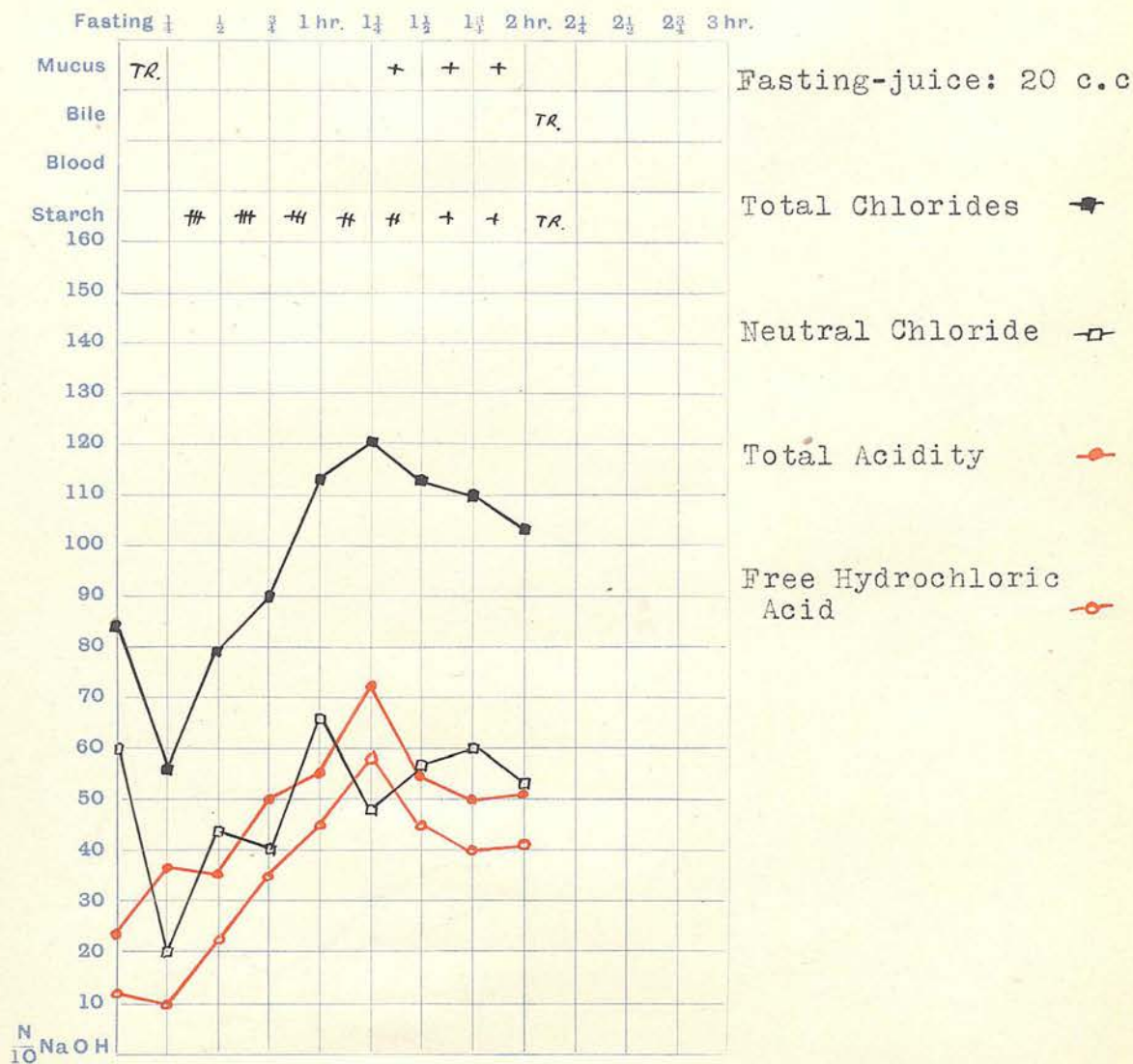
1. FRACTIONAL TEST-MEAL. Date 13. 12. '28.



Nil definite found at operation.

1. FRACTIONAL TEST-MEAL.

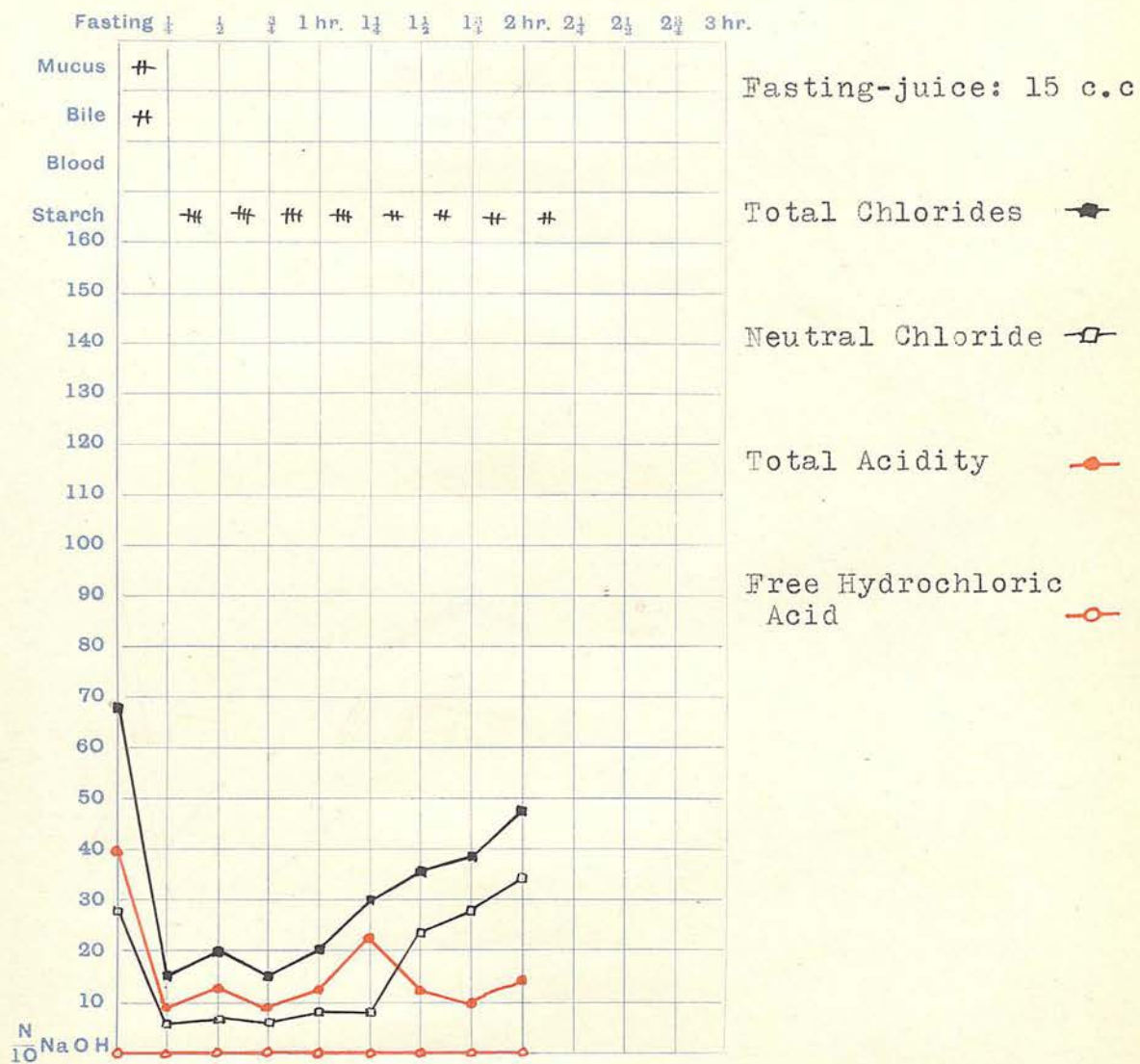
Date 14. 12. '28.



Nil definite found at operation.

1. FRACTIONAL TEST-MEAL.

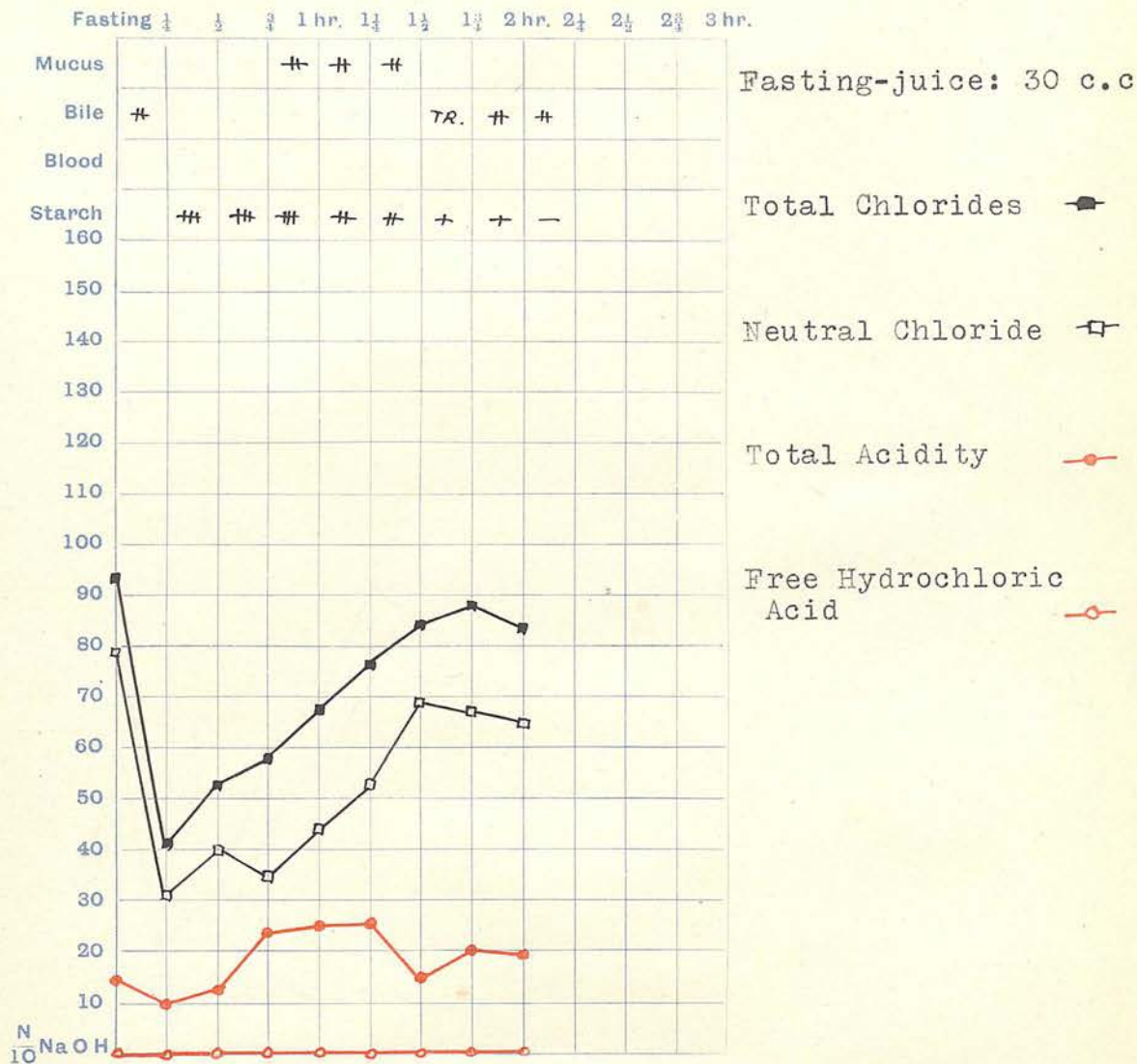
Date 30. 4. '28.



Nil definite found at operation.

Name of Patient F 6. (F. aet. 47)

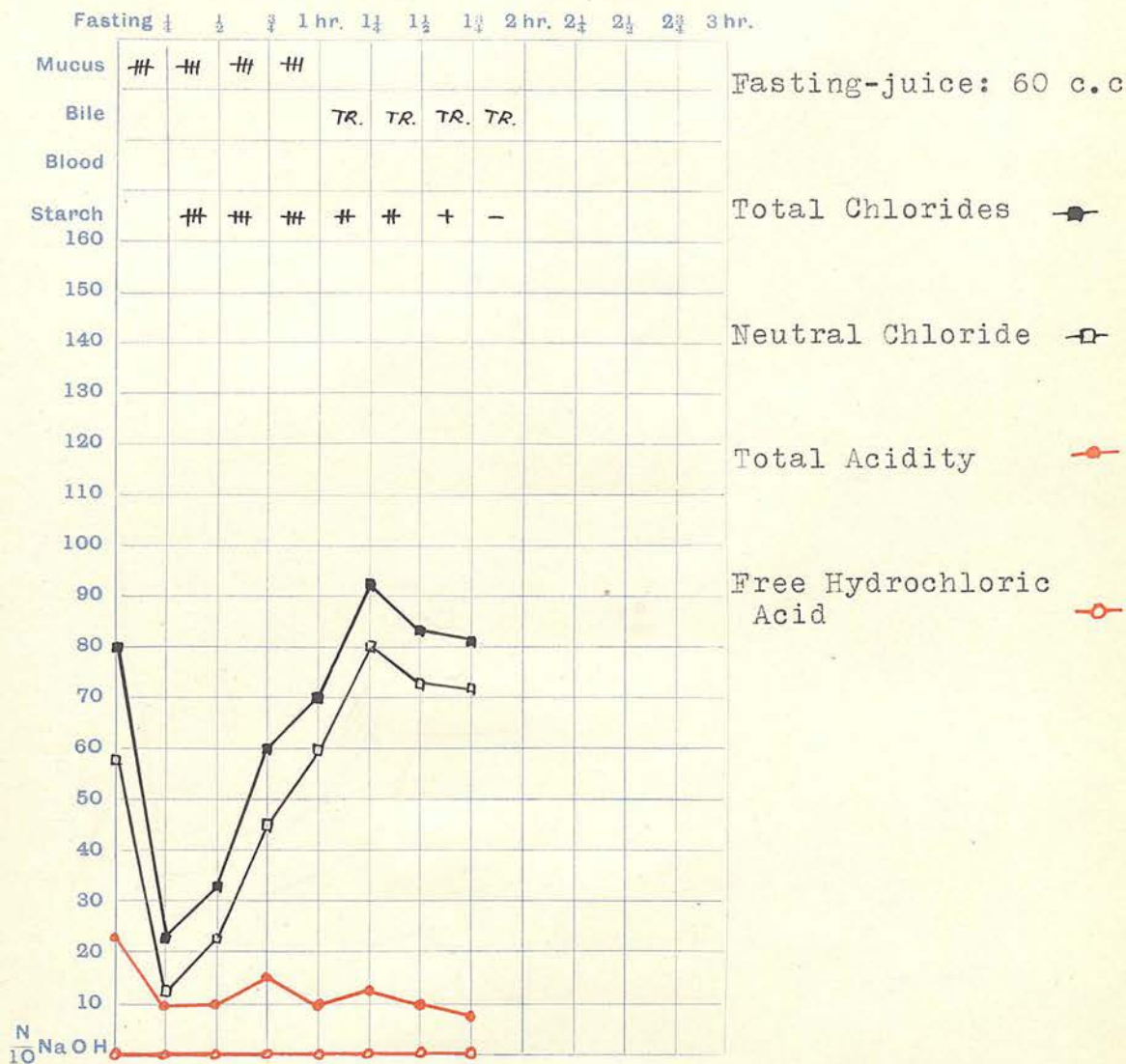
1. FRACTIONAL TEST-MEAL. Date 5. 5. '28.



Nil definite found at operation.

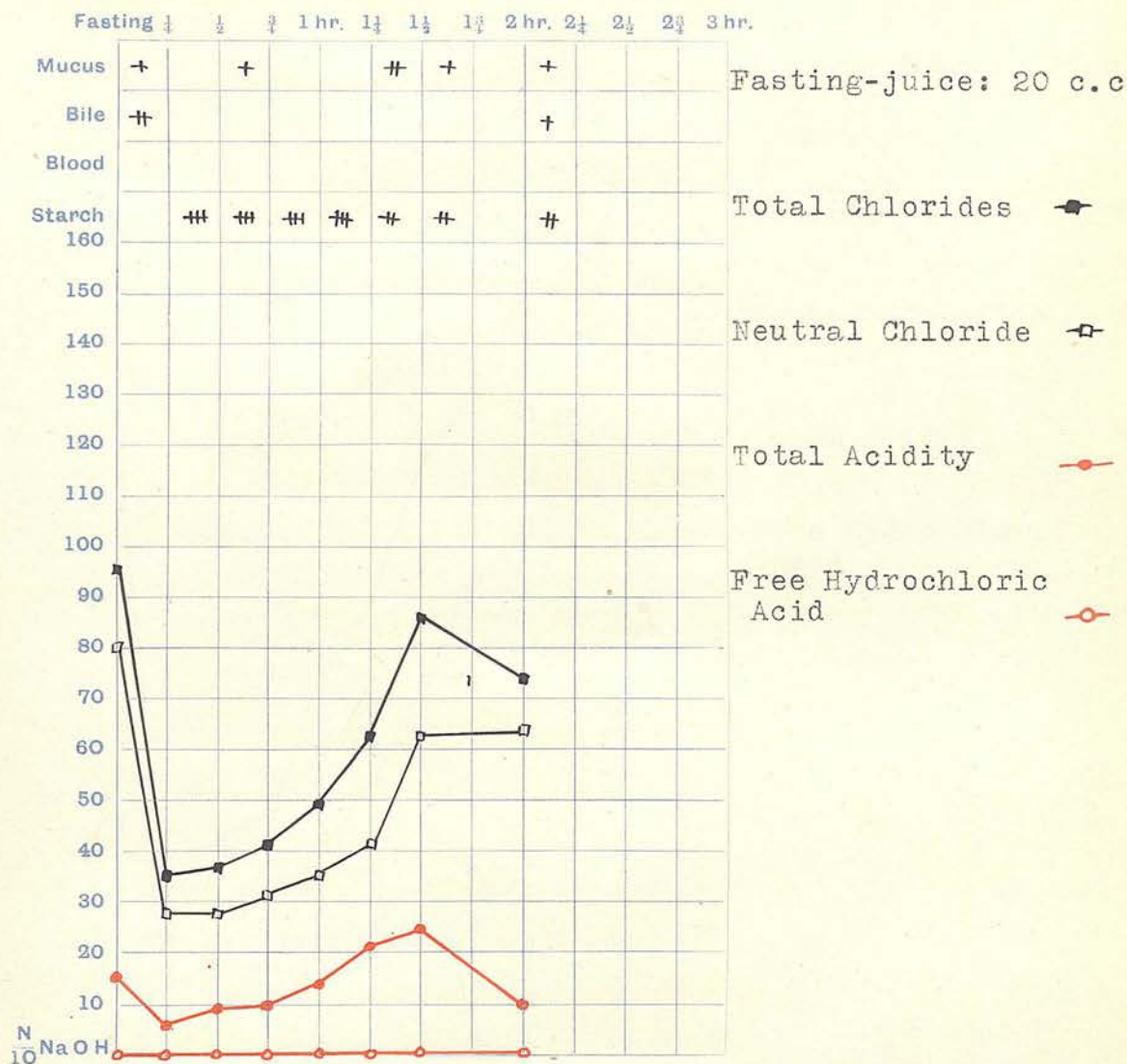
Name of Patient F 7. (F. aet. 21)

1. FRACTIONAL TEST-MEAL. Date 10. 7. '28.



Nil definite.

1. FRACTIONAL TEST-MEAL. Date 21. 5. '28.



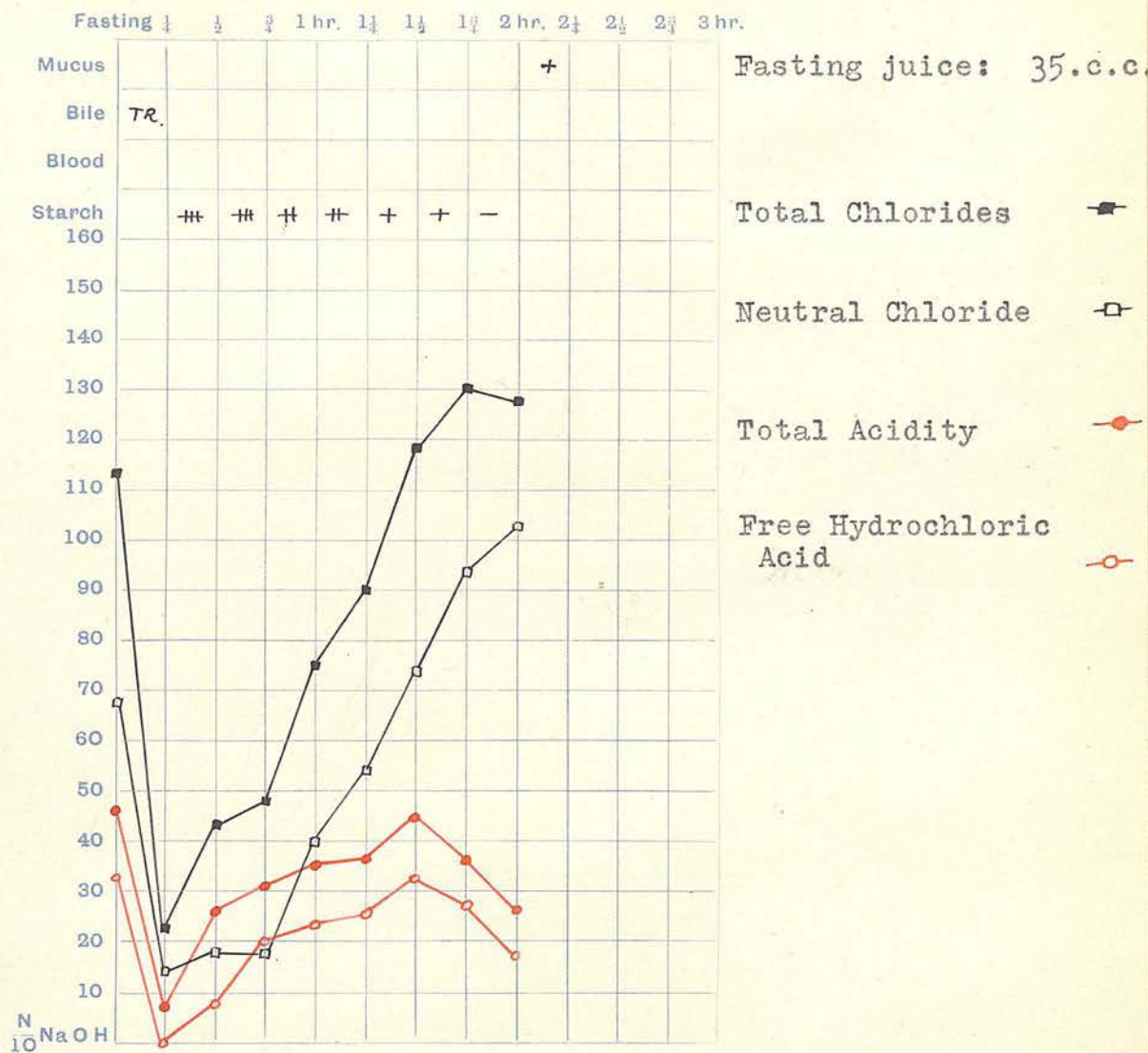
Nil definite.

Name of Patient F 9.

(F. aet. 45)

1. FRACTIONAL TEST-MEAL.

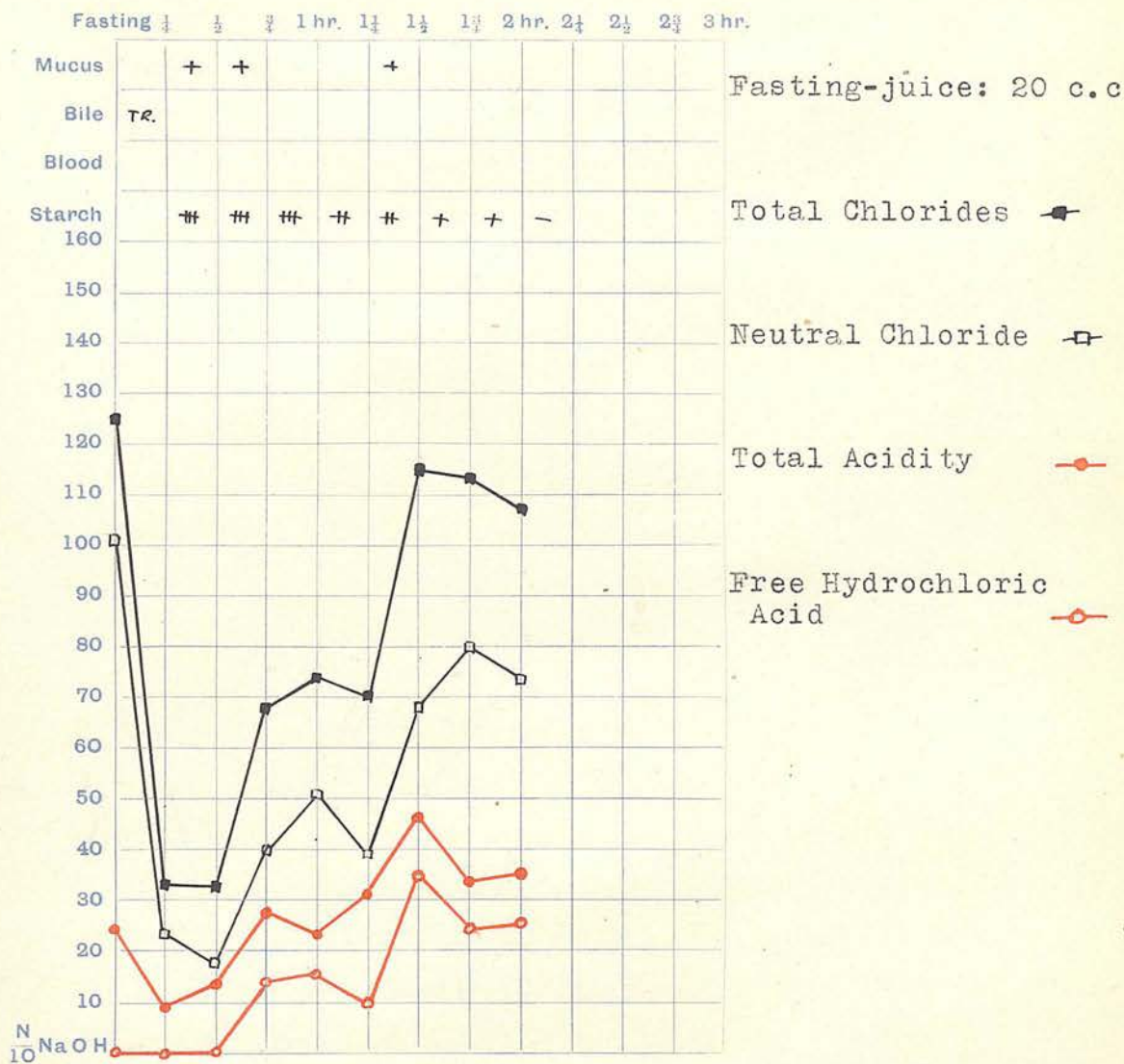
Date 28. 7. '28



Nil definite.

Name of Patient F 10. (F. aet. 43)

1. FRACTIONAL TEST-MEAL. Date 29. 6. '28.



Nil definite.

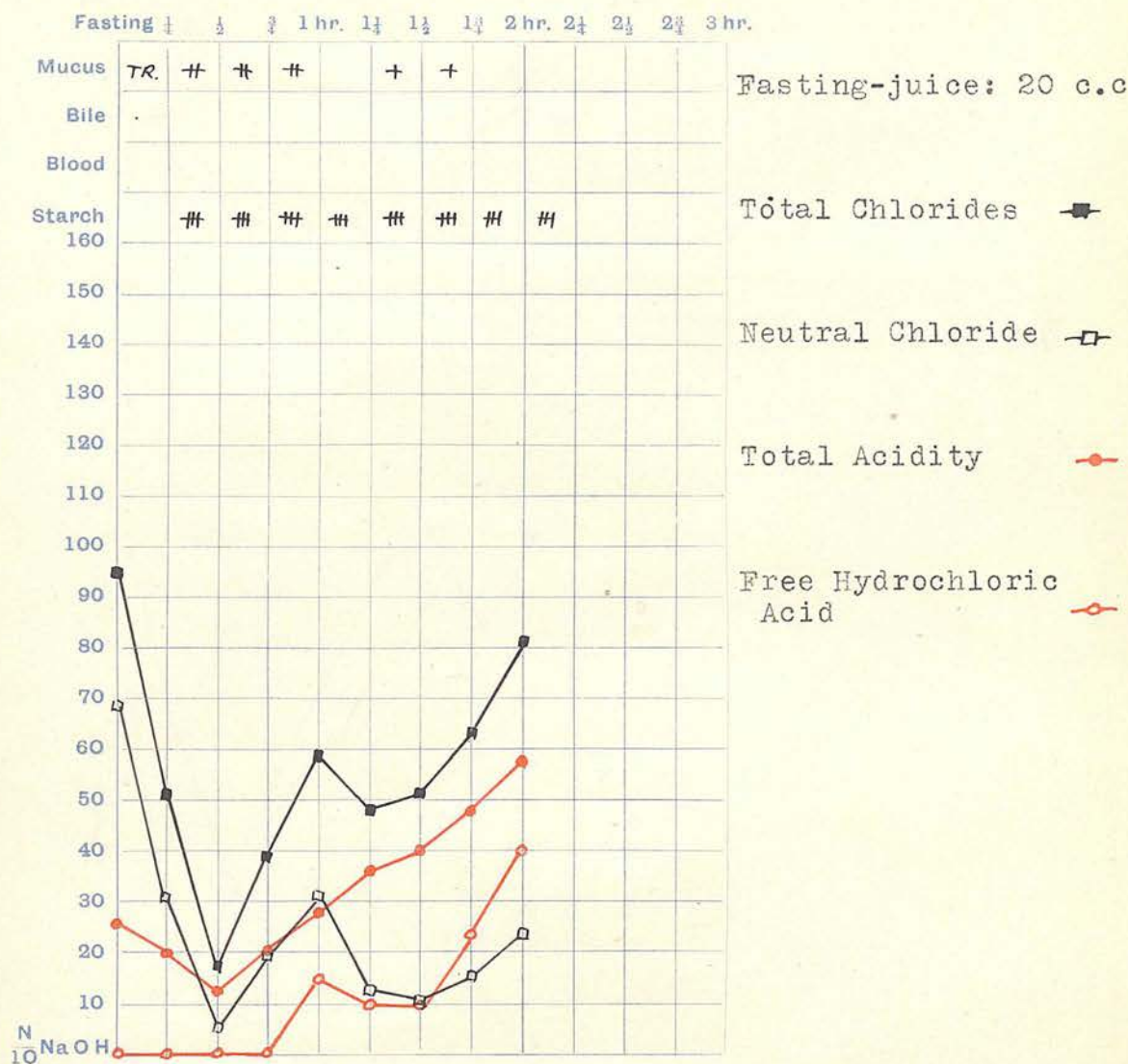
Name of Patient

F 11.

(M. aet. 47)

1. FRACTIONAL TEST-MEAL.

Date 22. 3. '29.



Nil definite.

Name of Patient

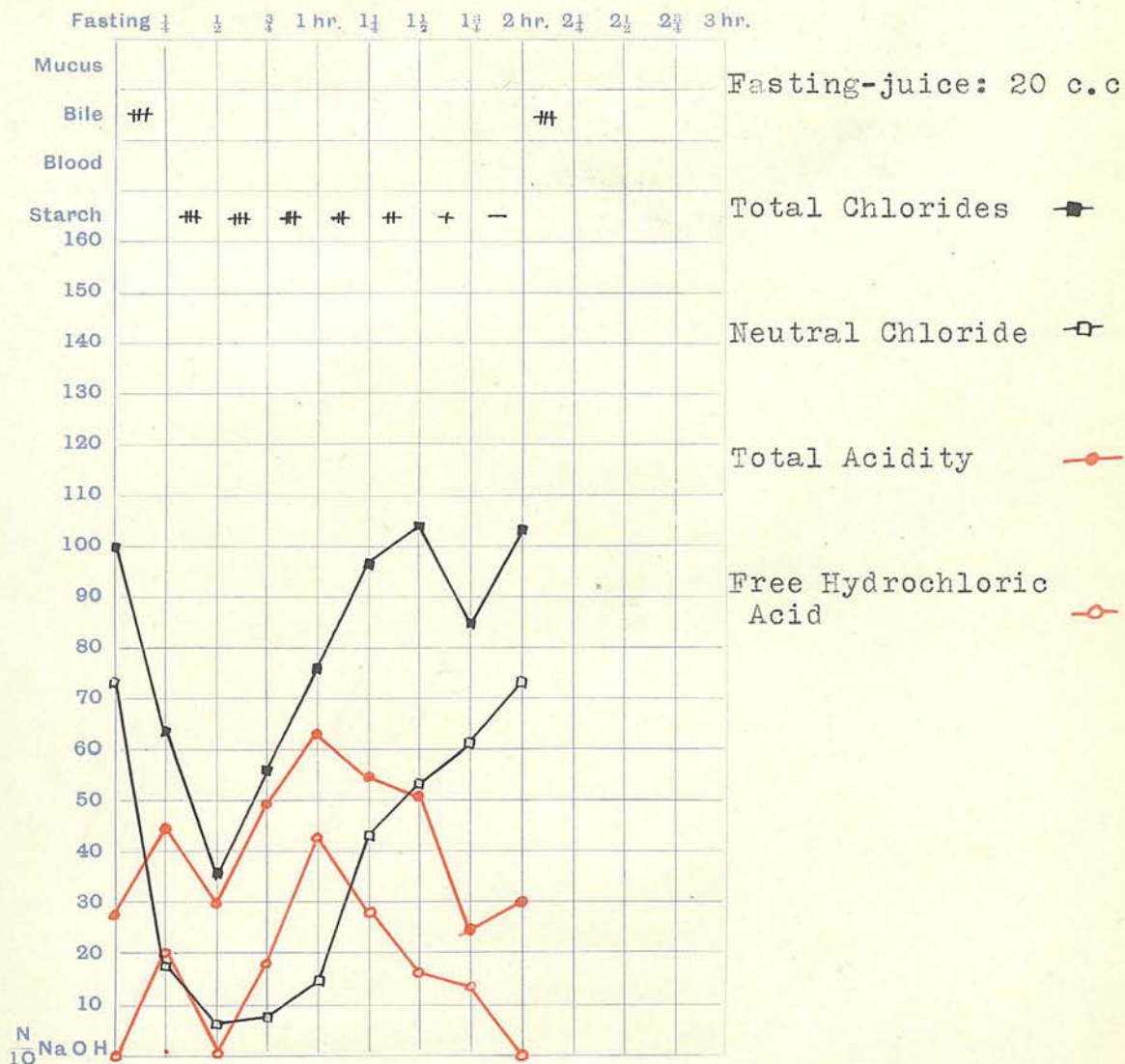
F

12.

(F. aet. 54)

1. FRACTIONAL TEST-MEAL.

Date 23. 7. '28.

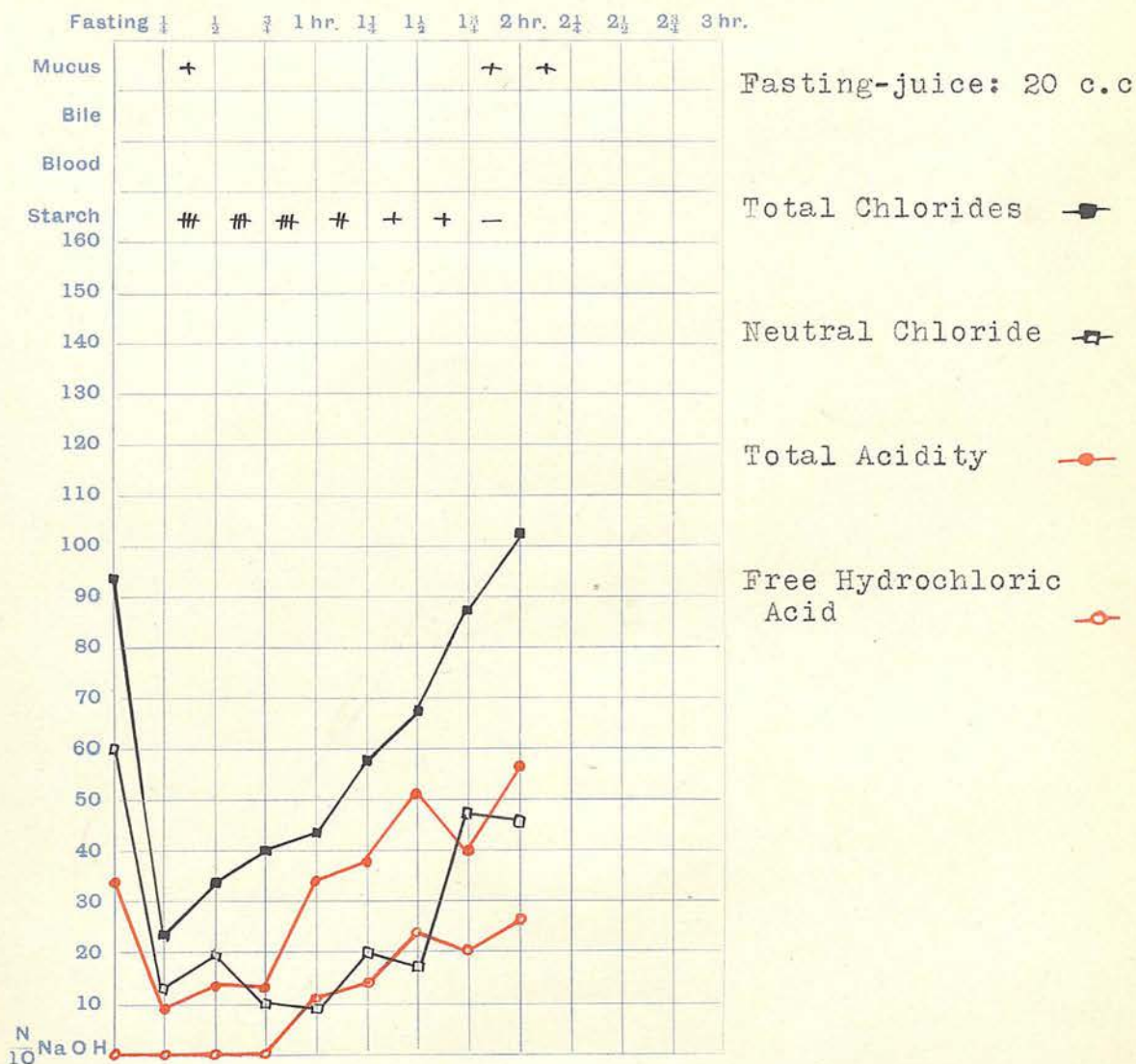


Nil definite.

Name of Patient F 13. (F. aet. 46)

1. FRACTIONAL TEST-MEAL.

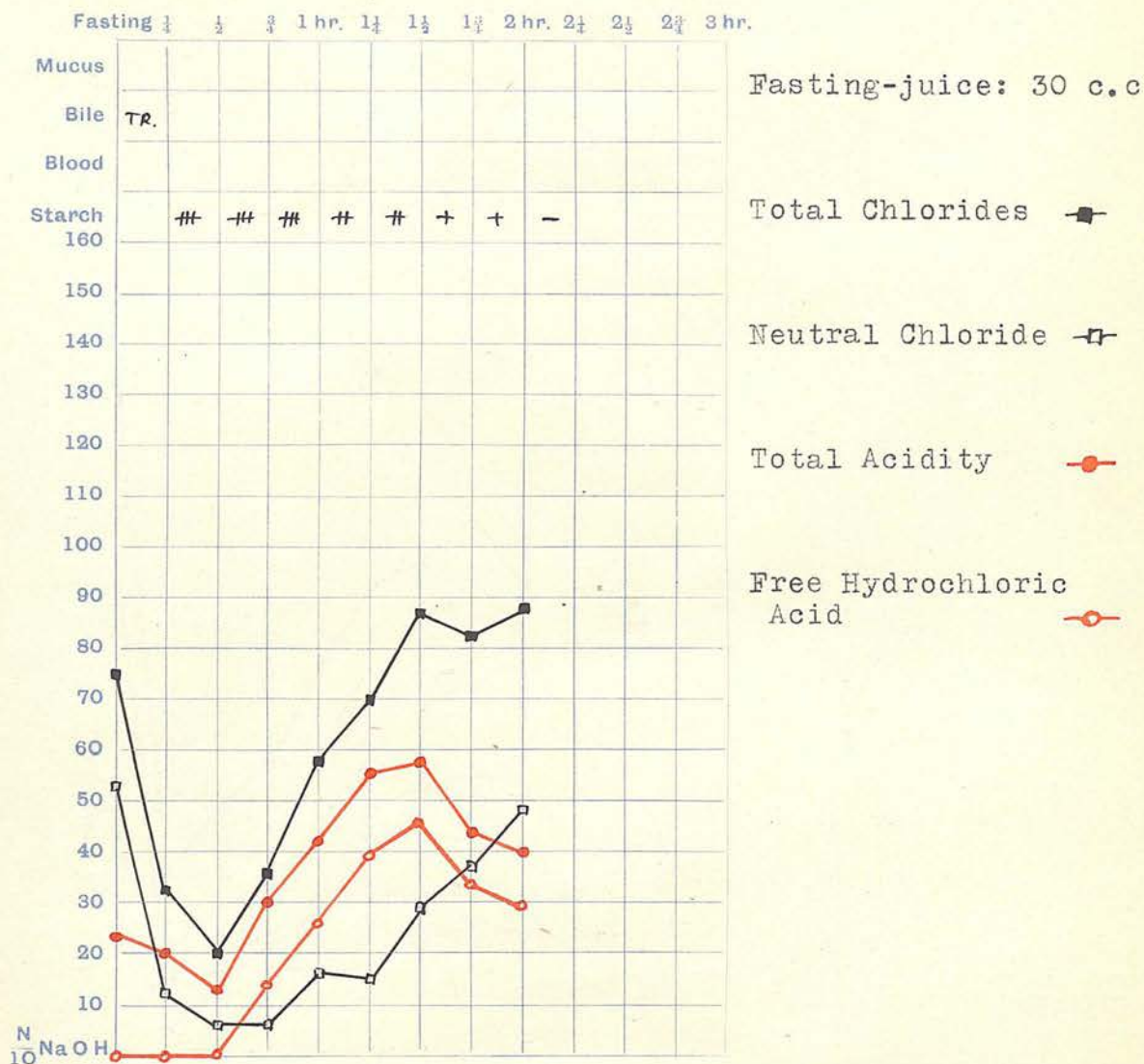
Date 18. 7. '28.



Nil definite.

Name of Patient F 14. (F. aet. 52)

1. FRACTIONAL TEST-MEAL. Date 29. 6. '28.



Nil definite.

Name of Patient

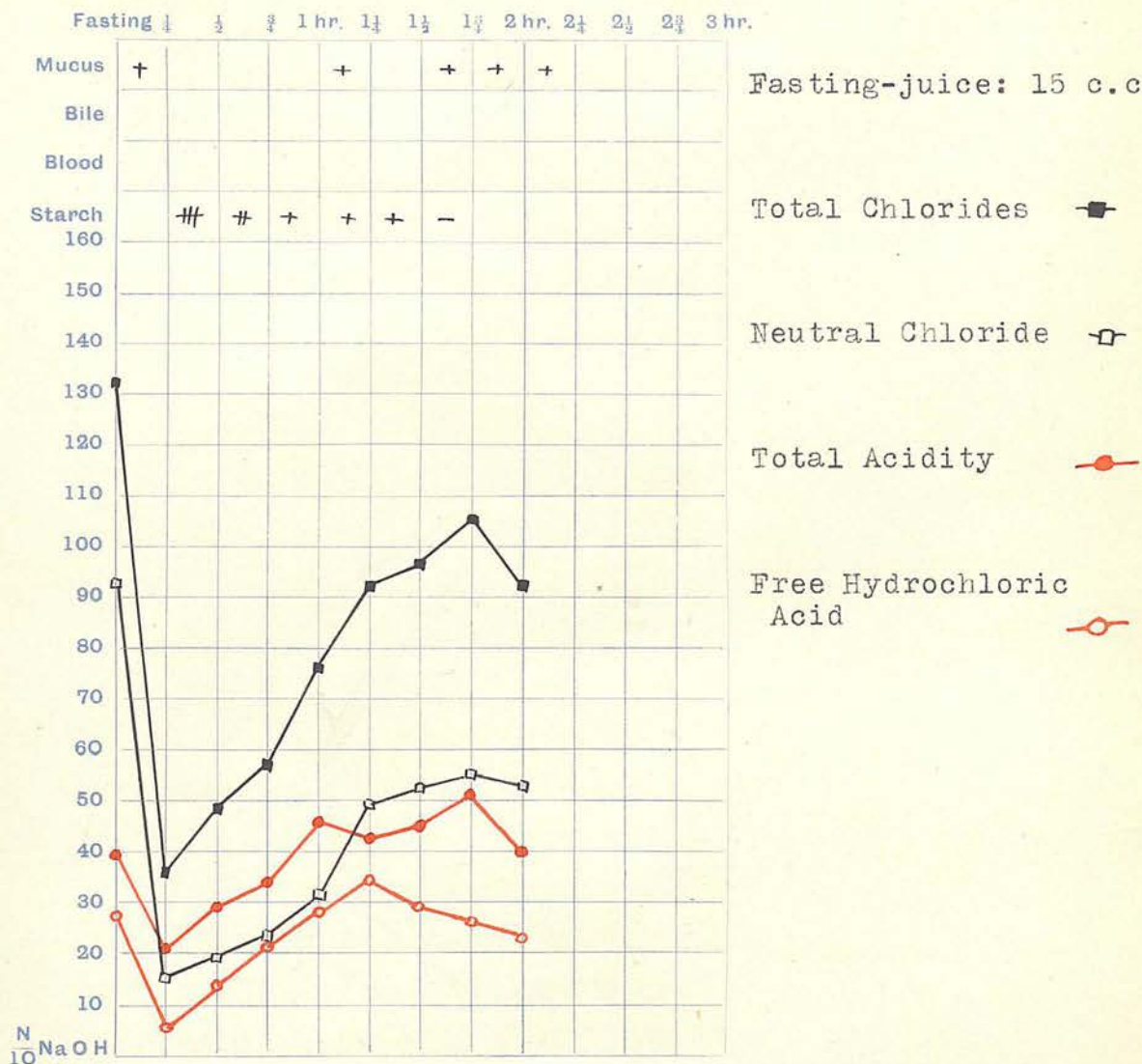
F

15.

(F. aet. 27)

1. FRACTIONAL TEST-MEAL.

Date 16. 6. '28.

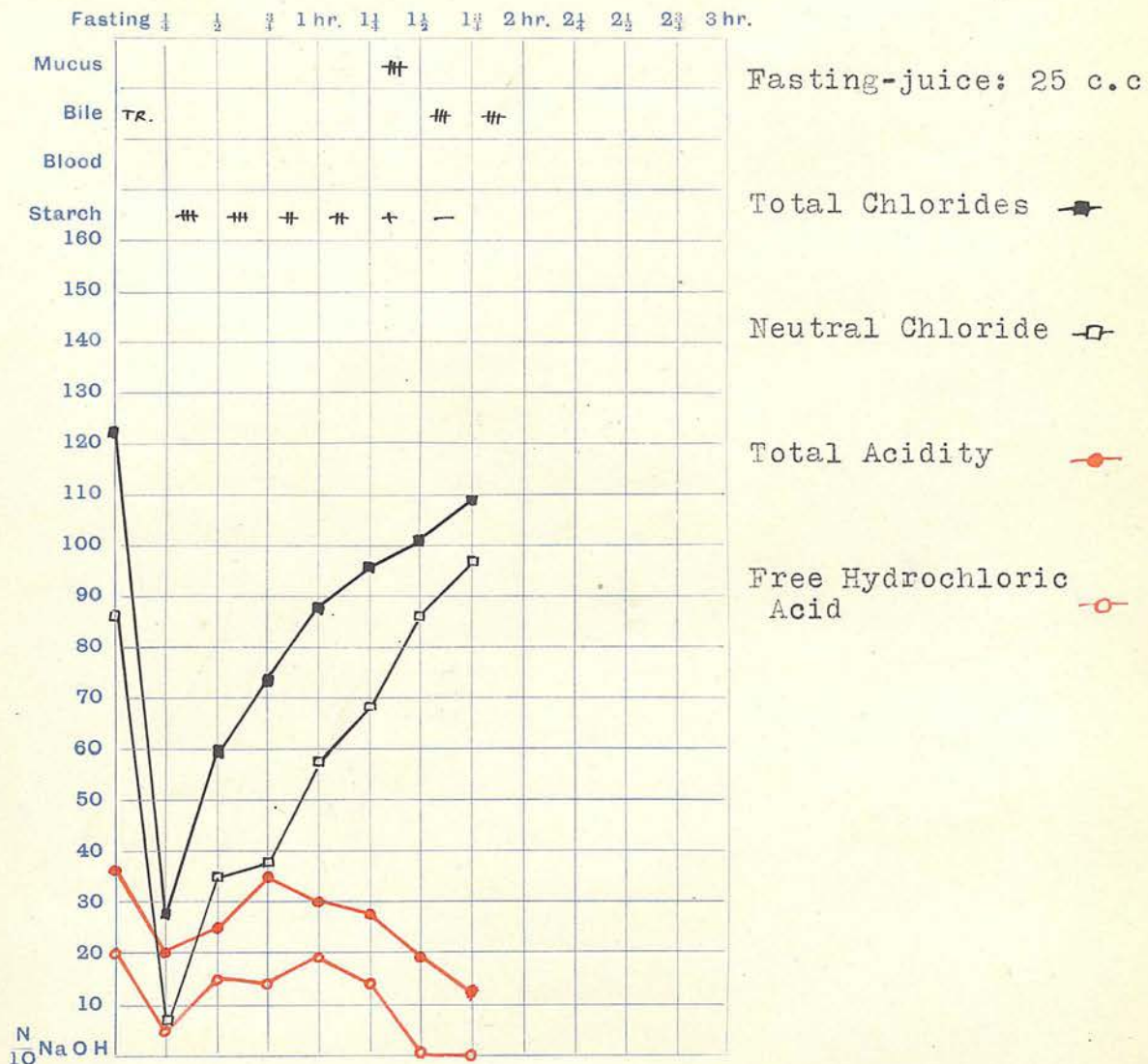


Nil definite.

Name of Patient F 16. (F. aet. 29)

1. FRACTIONAL TEST-MEAL.

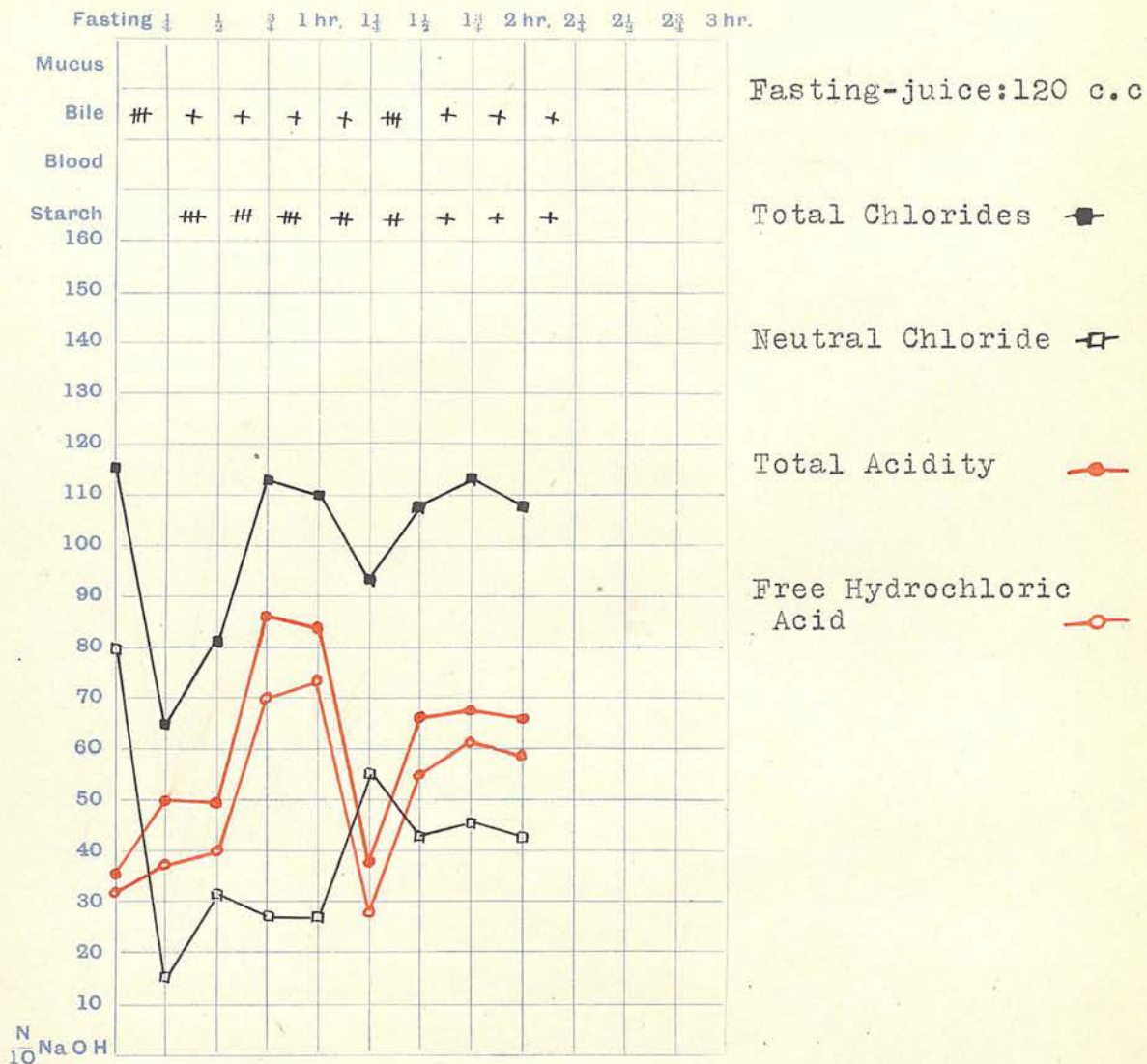
Date 3. 8. '28.



Nil definite.

Name of Patient M 1. (M. aet. 30)

1. FRACTIONAL TEST-MEAL. Date 14. 5. '29.

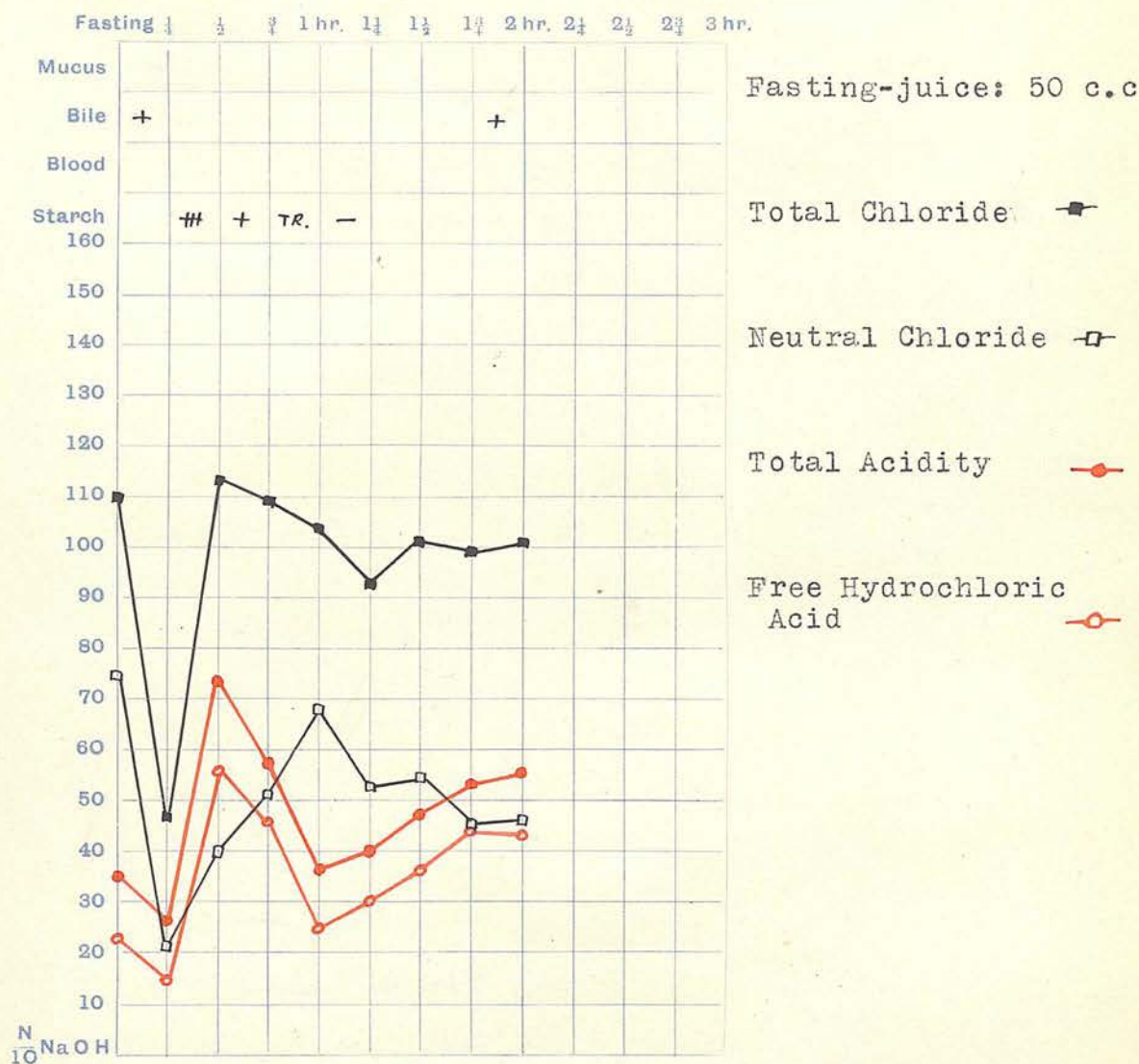


Duodenal ulcer: gastro-enterostomy two years ago.

Renewal of symptoms for last two months.

Name of Patient M 2. (M. aet. 38)

1. FRACTIONAL TEST-MEAL. Date 20. 5. '29.



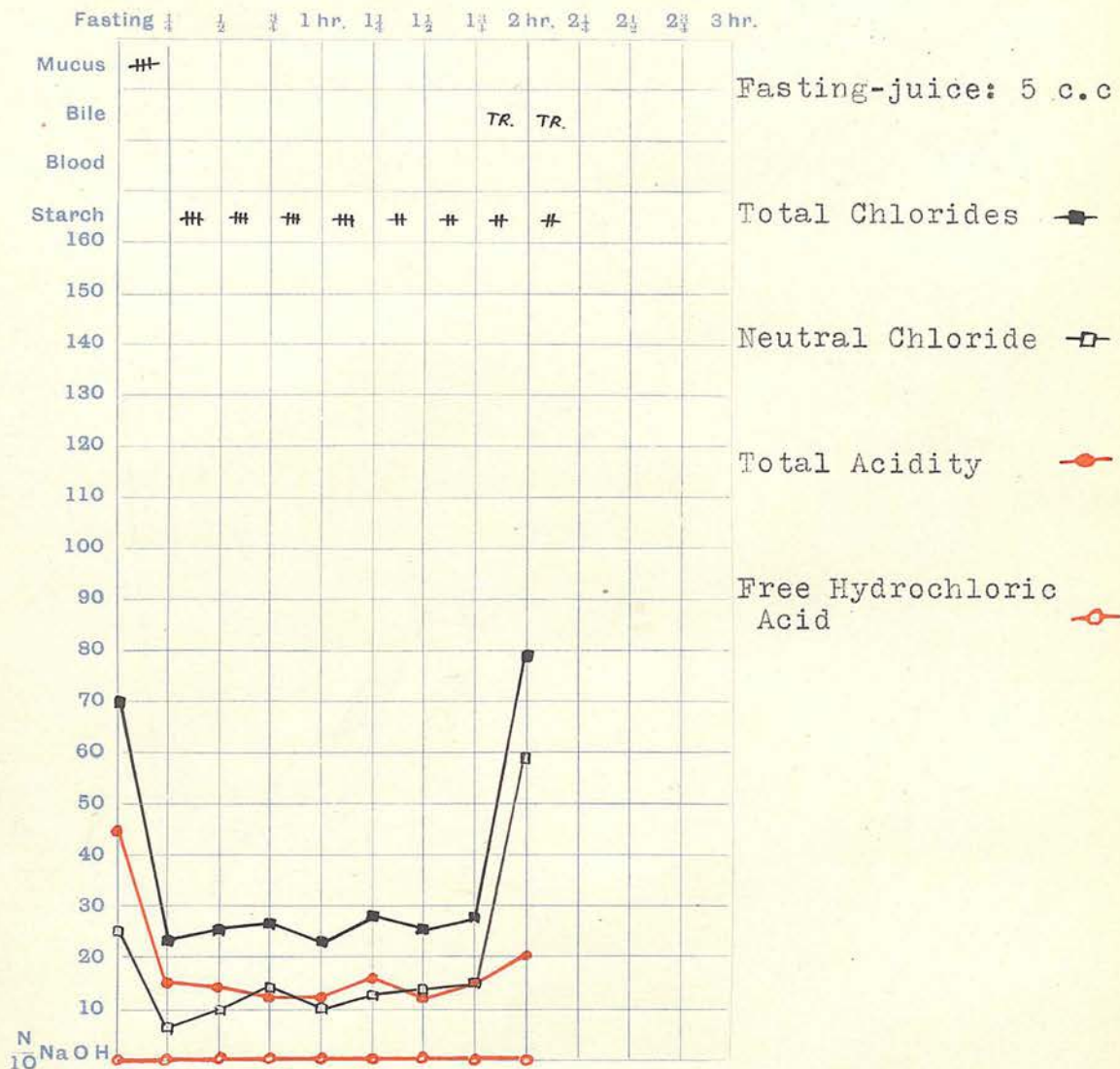
Multiple tuberculous strictures of small intestine.

Name of Patient M 3.

(M. aet. 47)

1. FRACTIONAL TEST-MEAL.

Date 2. 8. '28.



Carcinoma of head of pancreas.

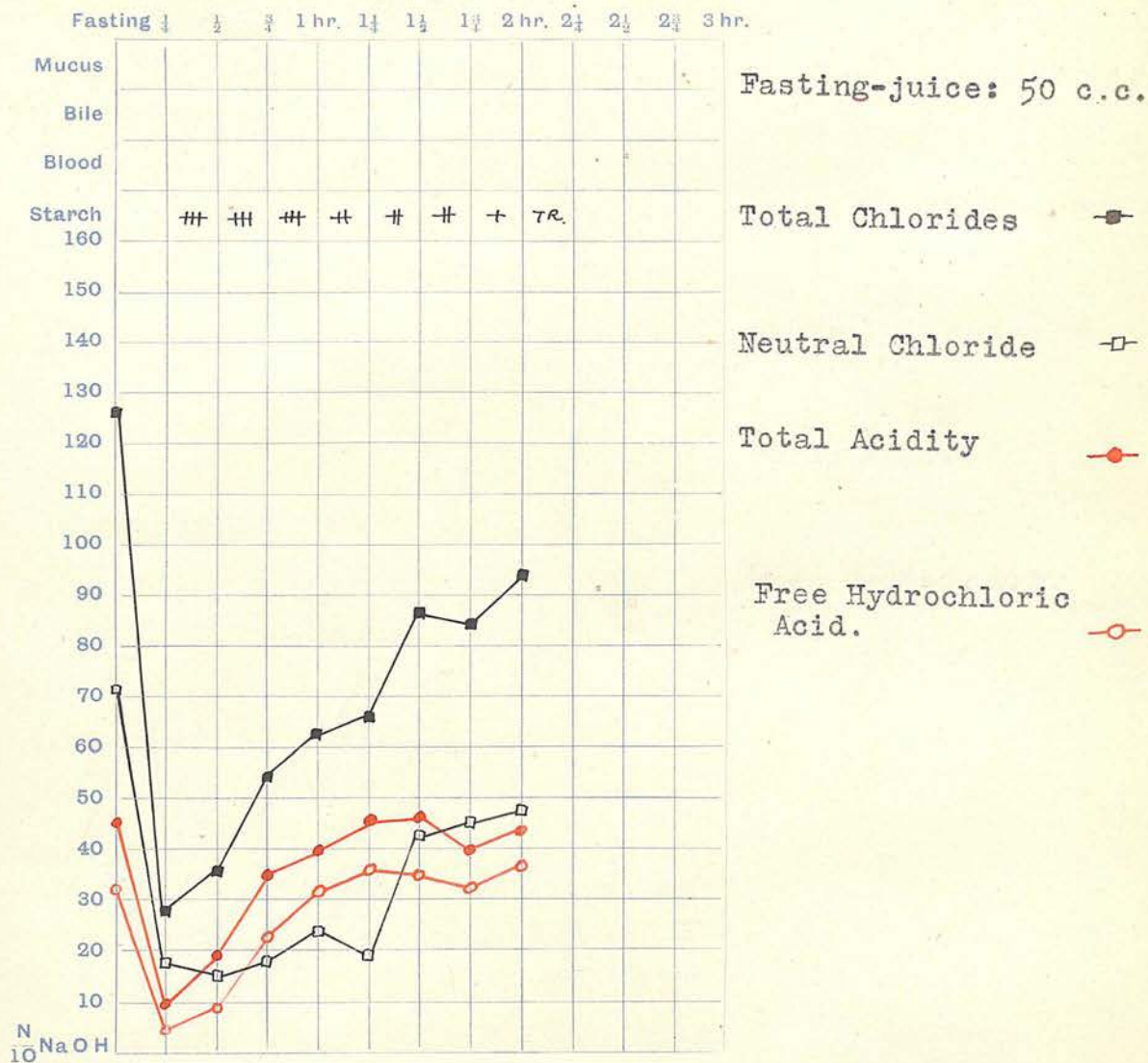
Name of Patient

M. 4.

(F. aet. 43)

1. FRACTIONAL TEST-MEAL.

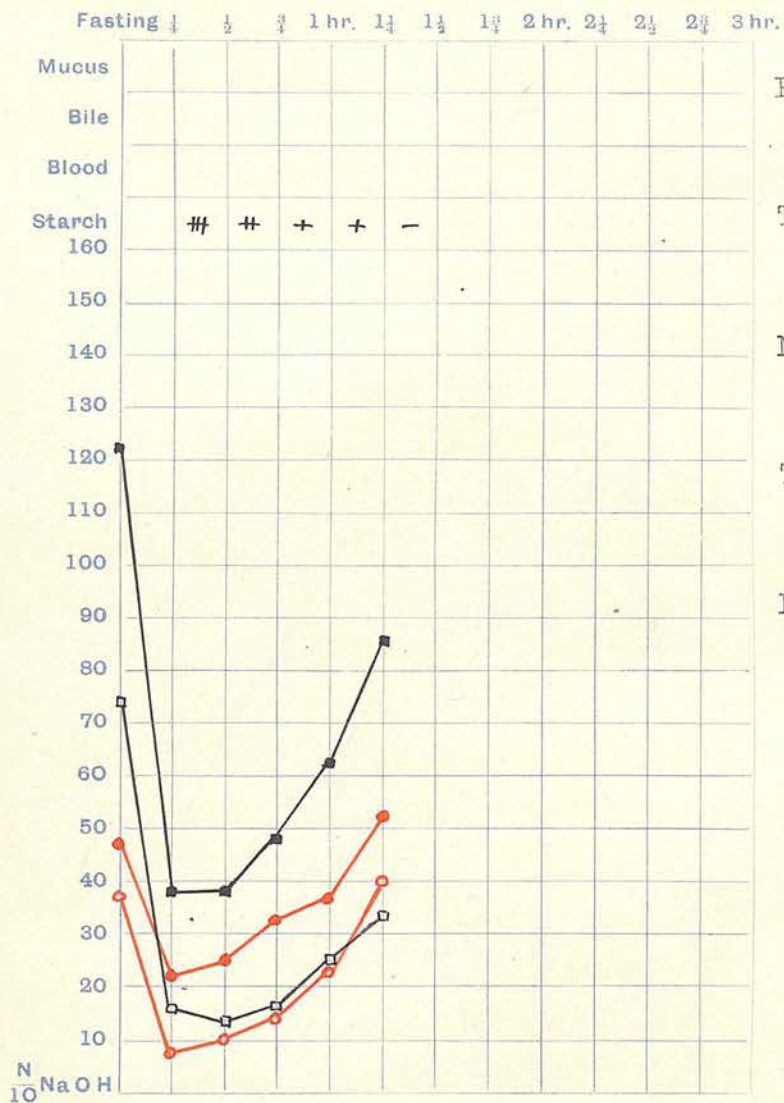
Date 27. 5. '29.



Carcinoma of head of Pancreas.

1. FRACTIONAL TEST-MEAL.

Date 27. 6. '28.



Fasting-juice: 30 c.c

Total Chlorides

Neutral Chloride

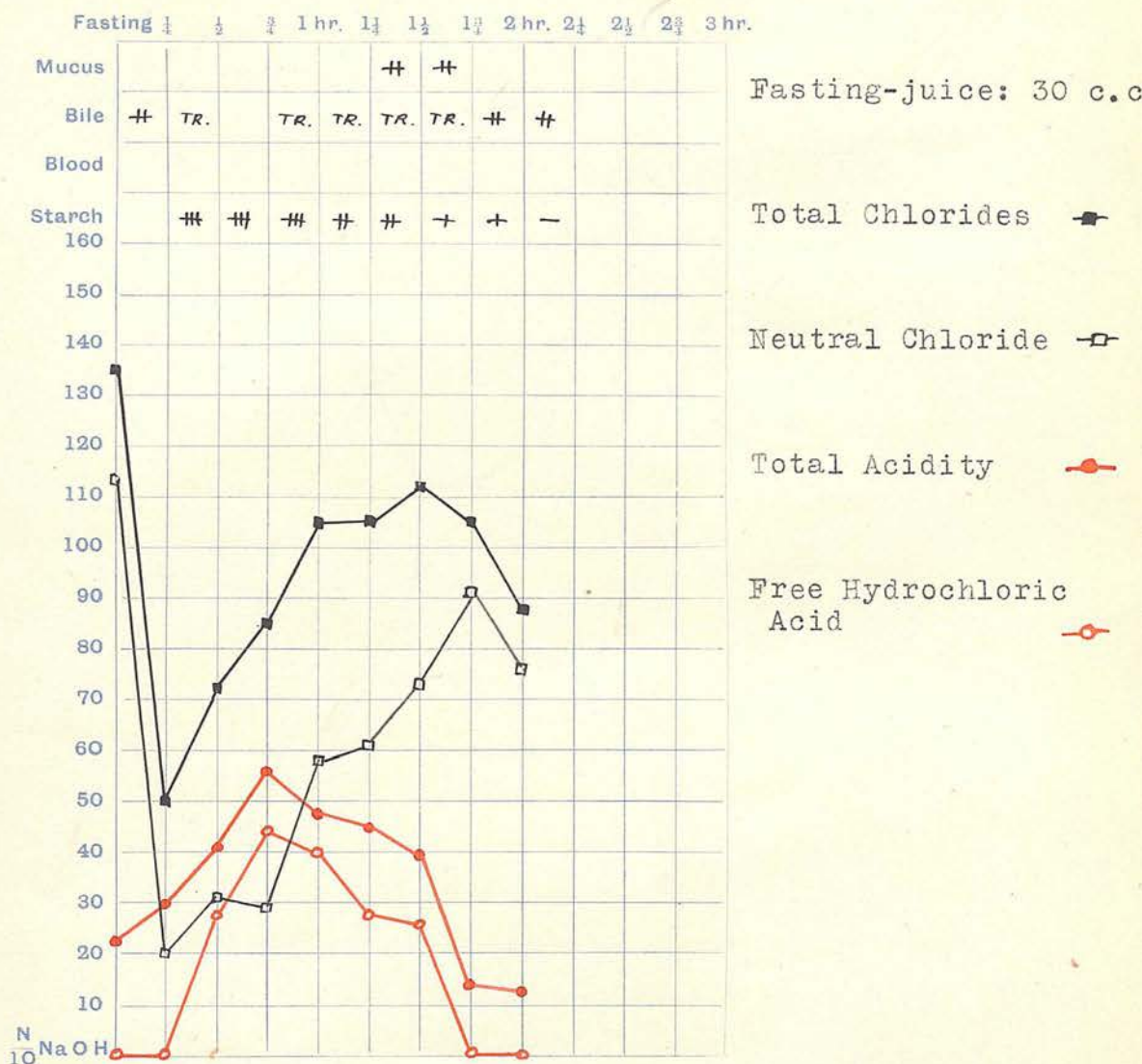
Total Acidity

Free Hydrochloric Acid

Chronic pancreatitis.

Name of Patient M 6. (M. aet. 27)

1. FRACTIONAL TEST-MEAL. Date 5. 6. '28.

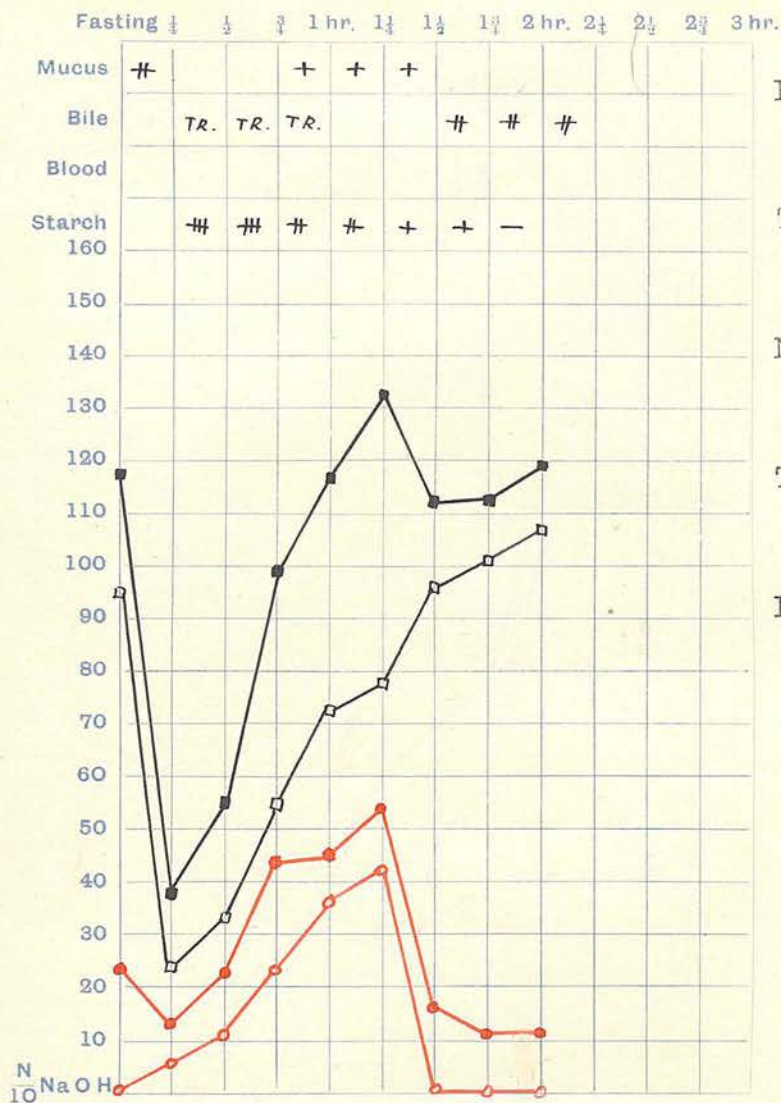


Catarrhal jaundice.

Name of Patient M 7. (M. aet. 48)

1. FRACTIONAL TEST-MEAL.

Date 21. 6. '28.



Fasting-juice: 20 c.c

Total Chlorides

Neutral Chloride

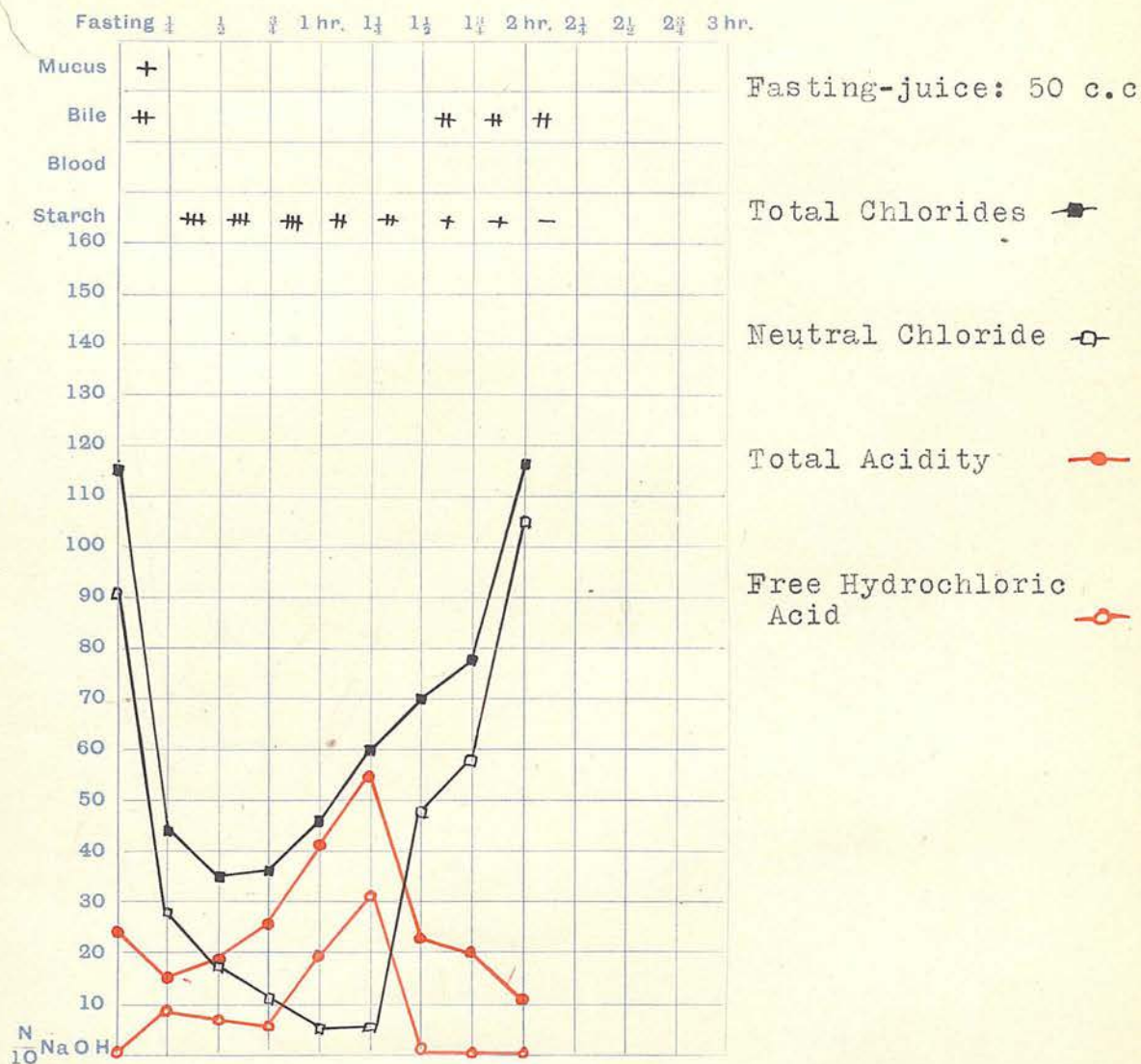
Total Acidity

Free Hydrochloric Acid

Spirochaetal cirrhosis of liver.

Name of Patient M 8. (M. aet. 46)

1. FRACTIONAL TEST-MEAL. Date 9. 5. '28.



Spirochaetal cirrhosis of liver.

Name of Patient

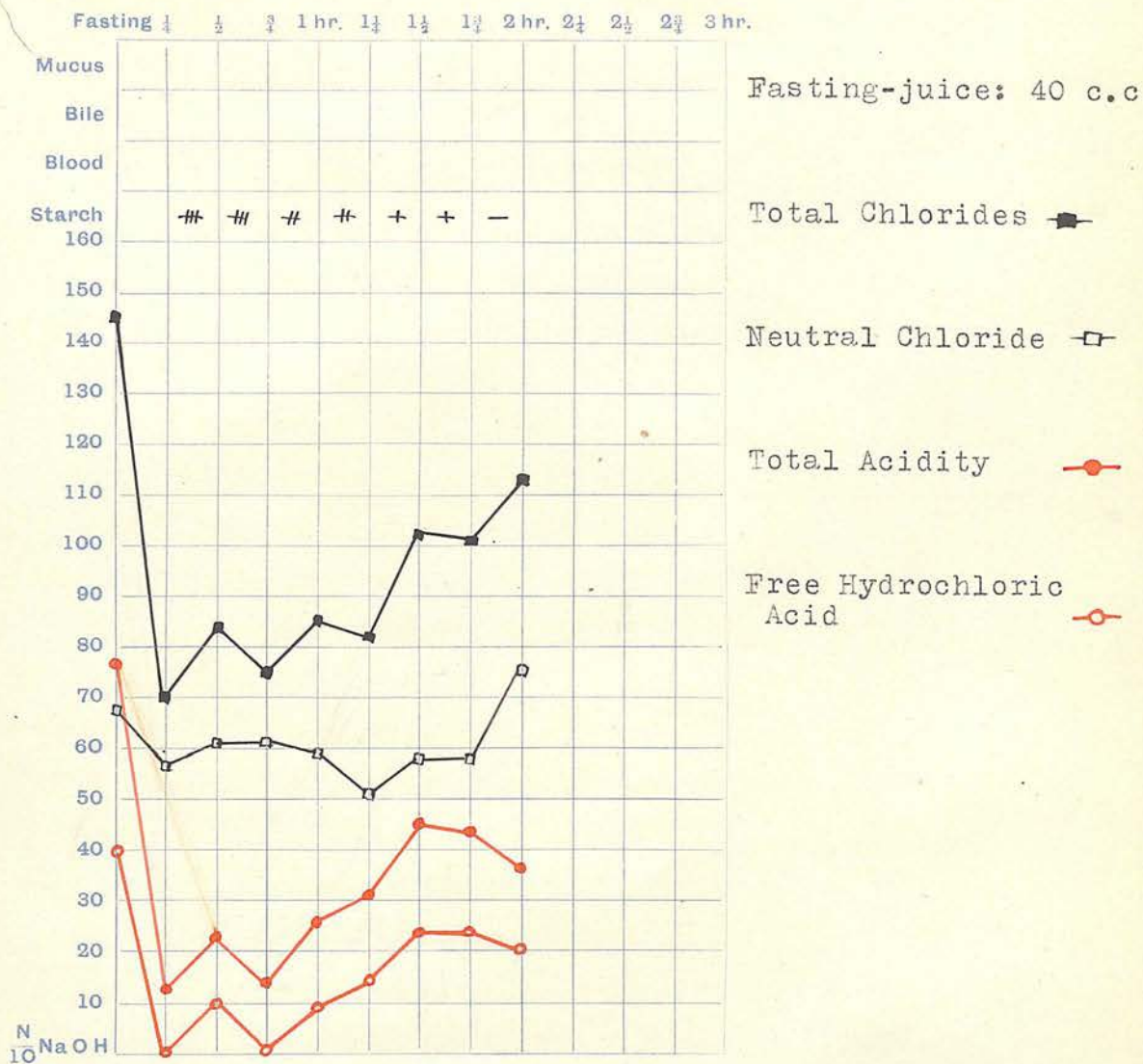
M

9.

(M. aet. 56)

1. FRACTIONAL TEST-MEAL.

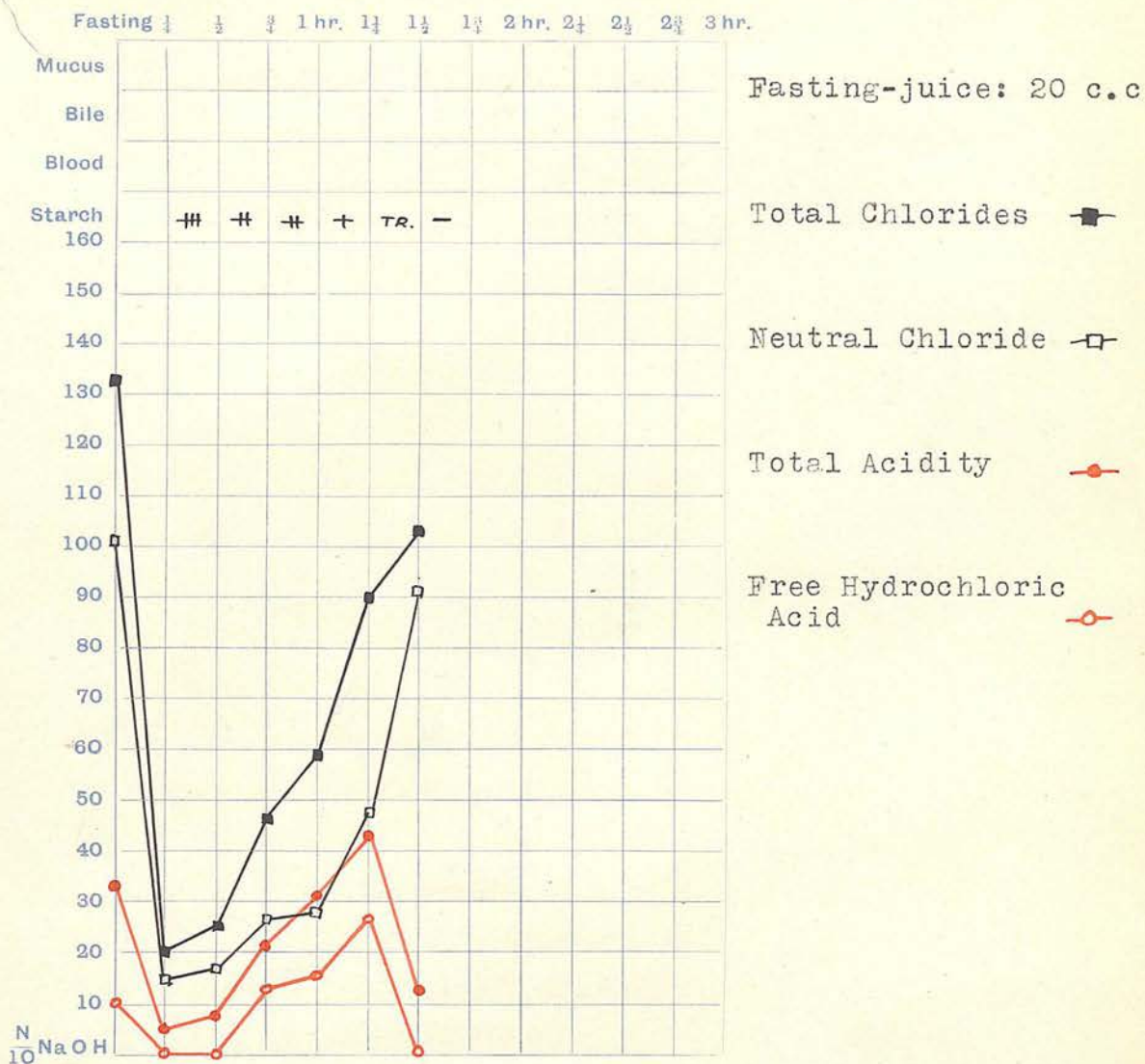
Date 20. 11. '28.



Malignant peritonitis.

Name of Patient M 10. (F. aet. 52)

1. FRACTIONAL TEST-MEAL. Date 22. 3. '29.



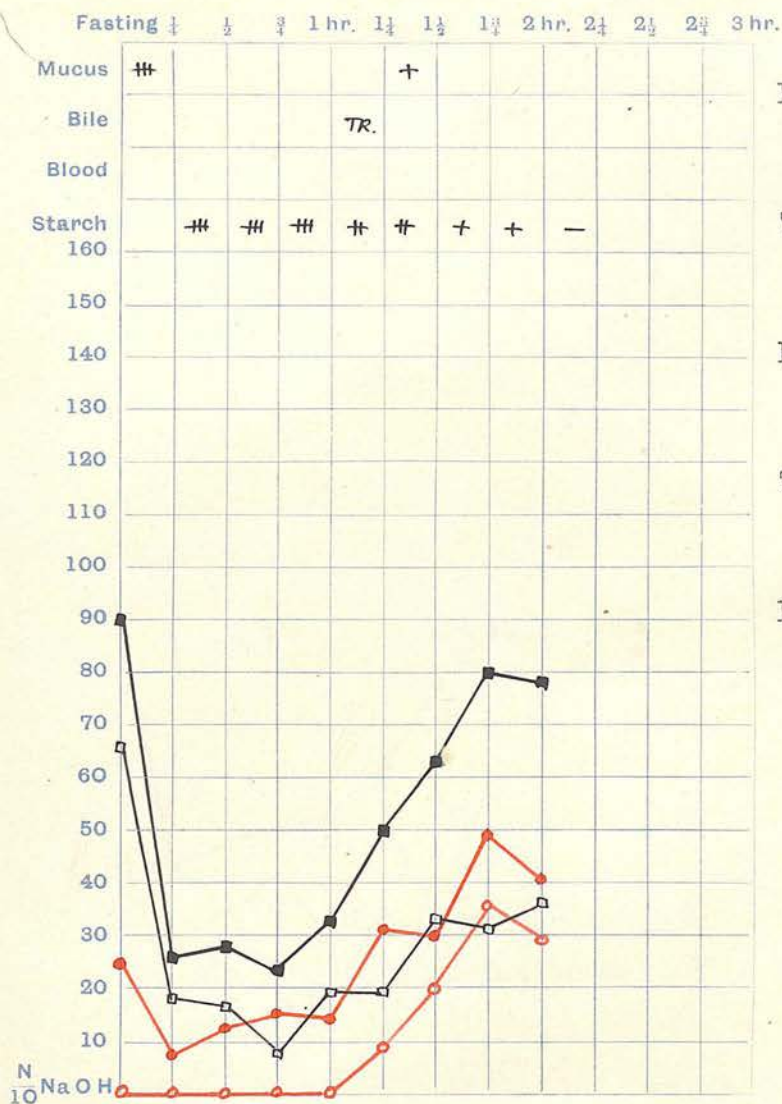
Malignant peritonitis.

Name of Patient M 11.

(F. aet. 48)

1. FRACTIONAL TEST-MEAL.

Date 2. 8. '28.



Fasting-juice: 20 c.c.

Total Chlorides —■—

Neutral Chloride —□—

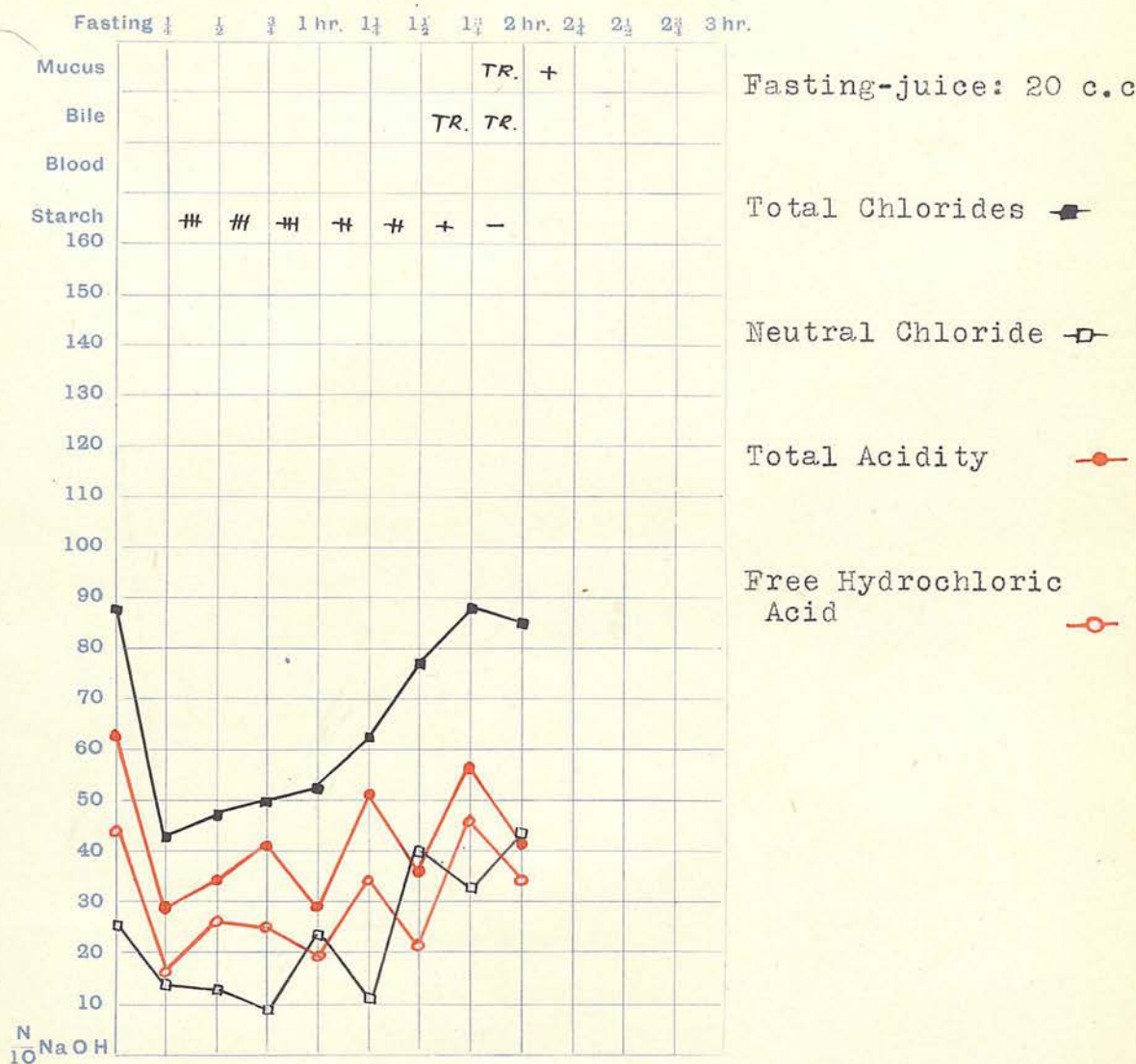
Total Acidity —●—

Free Hydrochloric Acid —○—

Carcinoma of caecum.

Name of Patient M 12. (M. aet. 28)

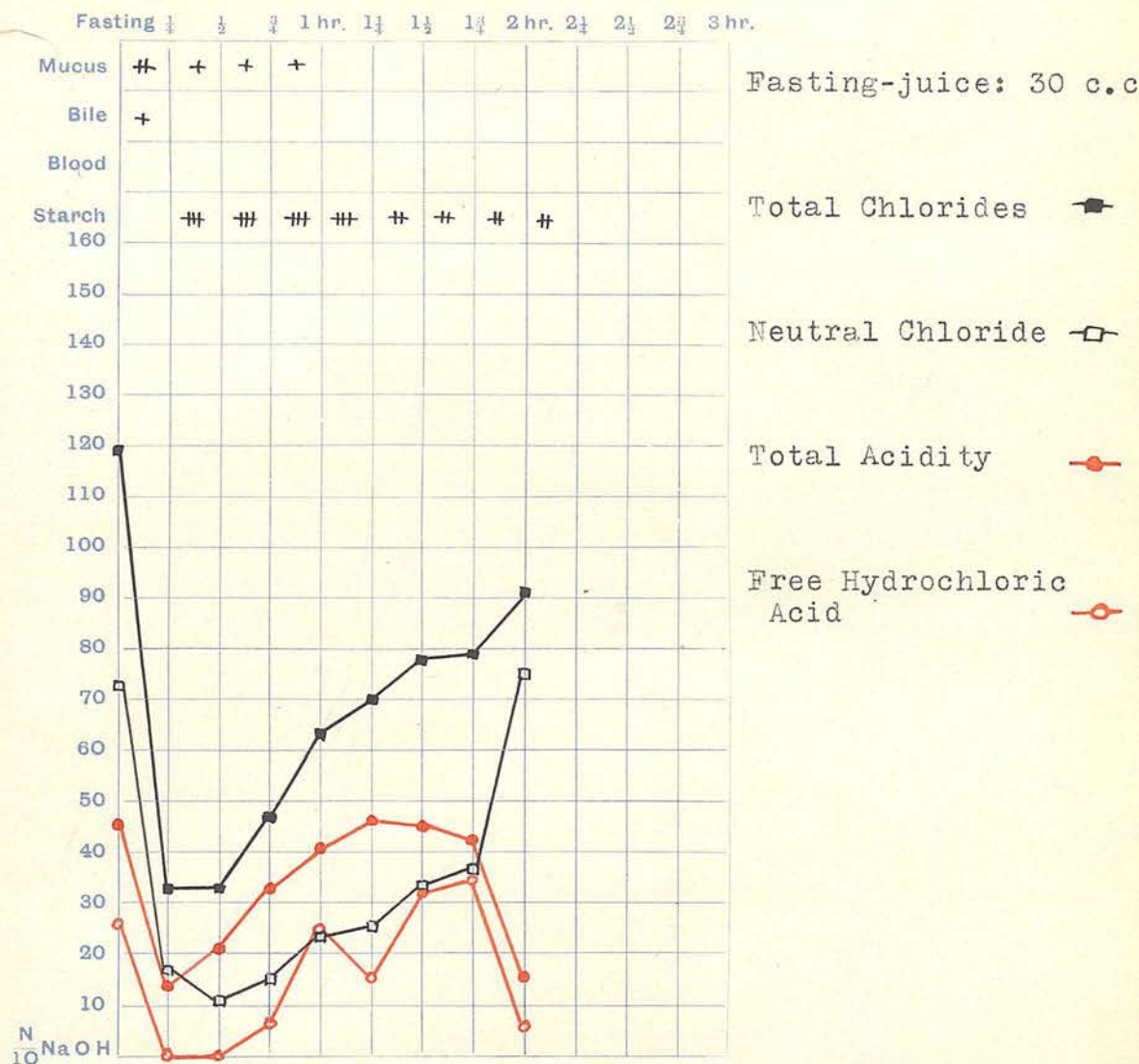
1. FRACTIONAL TEST-MEAL. Date 28. 7. '28.



Carcinoma of pelvic colon.

Name of Patient M 13. (F. aet. 36)

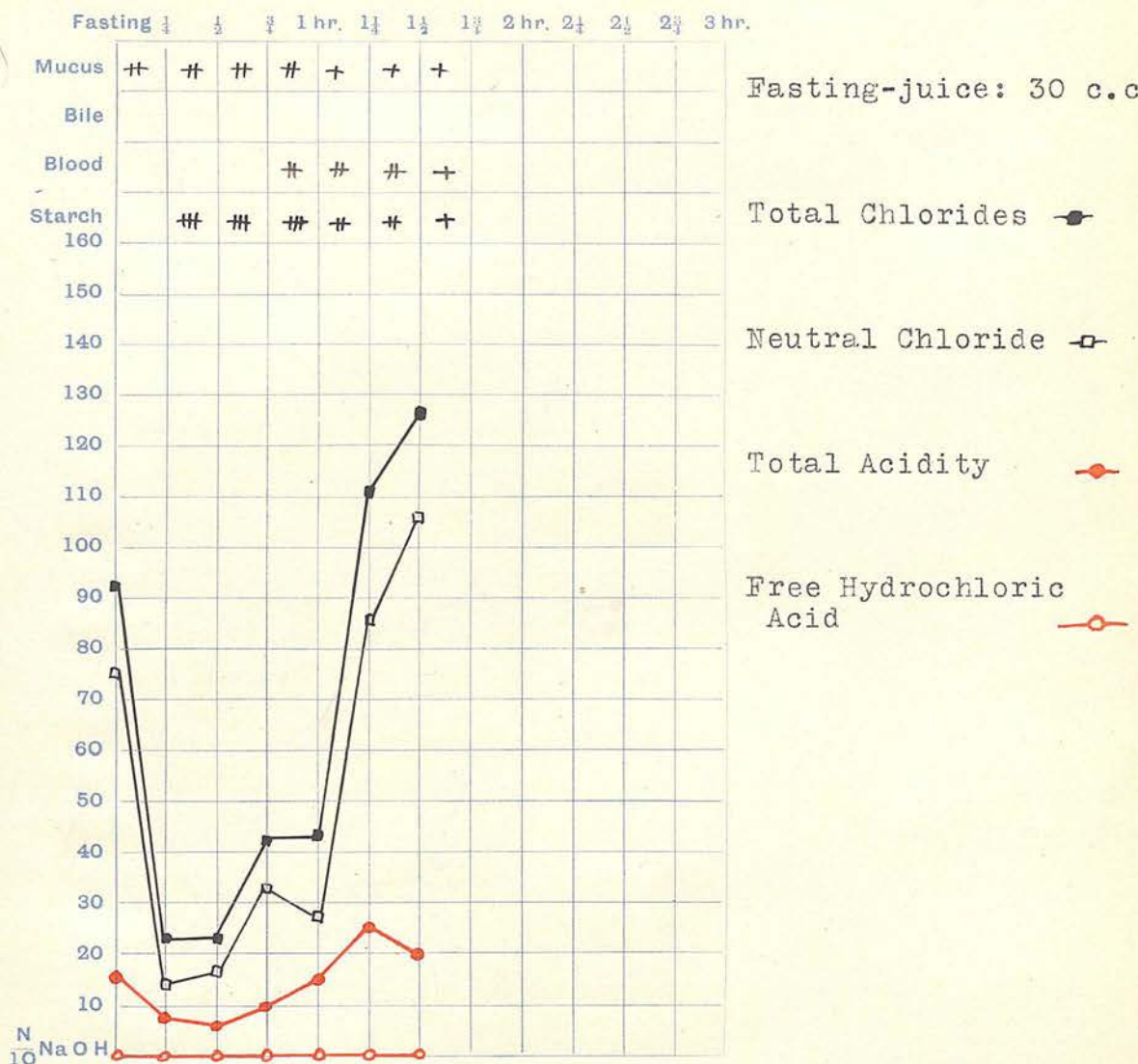
1. FRACTIONAL TEST-MEAL. Date 27. 5. '28.



Renal calculus (non-operated).

Name of Patient M 14. (F. aet. 45)

1. FRACTIONAL TEST-MEAL. Date 9. 9. '28.



Petit mal.

Name of Patient

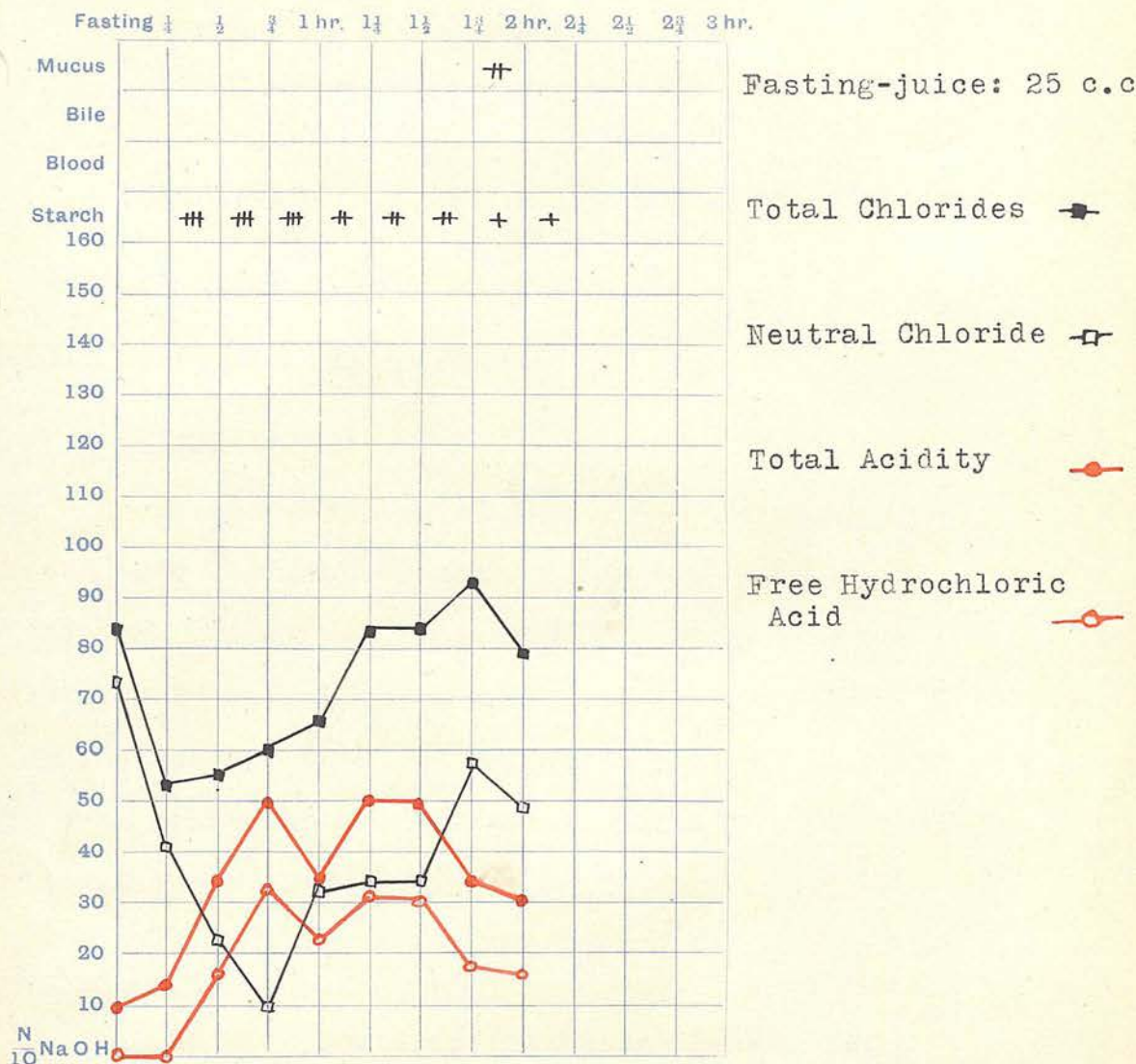
M

15.

(M. aet. 40)

1. FRACTIONAL TEST-MEAL.

Date 12. 2. '29.



Chronic iritis.

A P P E N D I X.

DESCRIPTION OF ANIMAL EXPERIMENTS.

Choice of experimental subject:-DOG A:- MALE.

An oesophageal tube (size 18) was passed into the stomach and some of the contents withdrawn. Much mucus was found; 'free' hydrochloric acid was absent - confirmed by a negative GÜNZBERG test. 40 G. of dog biscuit were given and the tube passed $1\frac{1}{2}$ hours later. 'Free' hydrochloric acid was again absent. This animal was rejected.

DOG B:- FEMALE.

Stomach contents, withdrawn by the tube, contained much free HCl - this was confirmed by GÜNZBERG'S test. A meal of biscuit was then given and the contents examined $1\frac{1}{2}$ hours later; Free HCl was again present.

On two occasions a gruel meal was administered, specimens of gastric contents being obtained half-hourly, by means of the tube.

16. 5. '29. OPERATION - see diagrams.

On the morning of operation, a milk-feed was given.

Under aether-anaesthesia, a midline incision was made from xiphisternum to umbilicus; the recti muscles were separated and the peritoneum opened in the line of the incision. The stomach was brought into the wound and the remaining contents of the abdomen packed off with gauze wrung out in warm saline.

Curved clamps, three quarters of an inch apart, were applied in such a manner as to isolate a portion of the stomach adjacent to the greater curvature, from two to three and a half inches from the pylorus.

An incision was next made, between the clamps, through the whole anterior wall of the stomach; this incision was deepened through the mucous membrane only of the posterior wall. Mucous membrane was freed from sub-mucous layer in both proximal and distal segments in order to facilitate invagination of the mucosa.

The serous and muscular coats of the anterior wall were then sutured down to the exposed portion of the submucous layer of the posterior wall.

An incision was then made into the pouch
-formed/

formed and a self-retaining catheter, of PEZER type, introduced. A purse-string suture was inserted round the opening. Packs were removed and the stomach returned to the abdomen. Interrupted sutures were introduced to bring the pouch and anterior abdominal wall into close apposition.

The wound was then closed, the free end of the catheter being brought out through the line of incision.

Diagrams representing the steps of the operation will be found in this section.

POSTOPERATIVE NOTES.

The animal had recovered sufficiently in one week to resume normal diet. The discharge from the wound was mainly haemorrhagic at first but gradually cleared.

The catheter became detached within three days of operation but the track remained patent. The wound was kept well lubricated with 'borated-lanolin' to prevent erosion of the skin edges. Later the application of a 5% aqueous solution of tannic acid proved useful in preserving the skin around the track.

The first investigation was carried out two weeks after operation.

A lubricated catheter was inserted as far as possible into the opening. The animal was then supported in a special wooden frame (see photographs). Food (100 G. meat) was administered and the secretion was collected in test-tubes, changed every quarter of an hour. At the end of two hours, by which time secretion was scanty, the catheter was removed and the animal then permitted to return to its cage.

Throughout this and other experiments the animal appeared indifferent to the requisite manipulative procedures.

Further investigations were performed in the same manner.

ANALYSIS OF SPECIMENS.

By the use of micro-methods, it was possible to estimate total chlorides, total acidity, neutral chloride and pepsin in 0.6 c.c. of secretion.

The total chlorides were estimated by the same methods as employed in the analysis of gastric contents.

For estimation of neutral chloride, the second method advocated by PATTERSON⁽⁵²⁾ was not found suitable. e.g., for two portions of the same specimen/

specimen, treated in the prescribed manner, the values 37 and 52 respectively were obtained.

Probably this variation was due to loss of chloride by volatilisation, although all recommended precautions were taken. The neutral chloride was obtained finally, as in the case of routine gastric analysis, by deducting total acidity from total chlorides.

Estimation of total acidity was performed by titrating 0.2 c.c. of secretion with N/50 NaOH, care being taken to prevent deterioration of the alkali from absorption of atmospheric carbon dioxide. Air, replacing alkali in the reservoir of the micro-burette, was rendered CO₂-free by passage through a U-tube containing fresh soda-lime.

The method was tested in regard to its reliability. 2 c.c. of a sample of gastric juice were titrated with N/10 alkali in the usual way; the acidity was found to be 46. Five samples of 0.2 c.c. were successively estimated by the new method.

The following burette-readings were obtained:- 0.47, 0.46, 0.46, 0.46, 0.45: mean 0.46. This corresponds to an acidity of 46, identical with that obtained by the previous method.

Pepsin was estimated, by the new method,
in/

in 0.2 c.c. of secretion, commencing with the 1 in 10 dilution.

Results are recorded in accompanying charts.

A second operation was performed for the purpose of obtaining, simultaneously specimens of gastric secretion from the upper and the lower parts of the fundus. An ordinary 'PAVLOV-pouch' was therefore constructed in addition to the existing low fundus-pouch.

20. 6. '29. OPERATION FOR 'PAVLOV-POUCH'.

A left paramesial incision was made from the costal margin to the level of the umbilicus; the left rectus muscle was split and the peritoneum opened in the line of the incision.

The stomach was exposed and the other organs packed off.

Straight clamps, separated by $\frac{5}{8}$ ", were applied to the stomach in such a manner as to permit of an axial incision through both anterior and posterior walls from a point on the greater curvature approximately $4\frac{1}{2}$ " from the pylorus.

The clamp on the flap was then removed and the bleeding-points ligatured.

The triangular flap thus formed, was opened out and an incision, through mucous membrane only/

only, was made at its base. The mucosa of both flap and main stomach were dissected up from the submucous layer sufficiently to allow of invagination.

The clamp on the main stomach was then removed and the cavity closed off by invagination of mucous membrane and serous and muscular coats. The flap was then formed into a tube, the distal end remaining open.

Packs were removed and the abdomen closed, the pouch being made to open externally in the line of incision.

POSTOPERATIVE NOTES:

Rapid recovery was noted for two days; thereafter progress became retarded, the animal refused all food requiring to be fed through an oesophageal tube.

Death occurred six days after the second operation; an immediate autopsy revealed the cause of death as pneumonia of the cardiac lobe of the right lung.

No evidence of peritonitis was found and healing in the recently-formed pouch had already proceeded sufficiently far to permit of distension with/

with barium sulphate emulsion in preparing skiagrams of the two pouches. No leakage was detected.

Photographs representing macroscopic and microscopic sections of the whole stomach and portions thereof are shown. Sections were stained with haematoxylin and eosin, and MALLORY'S stain; the latter, however, failed to show clear differentiation.

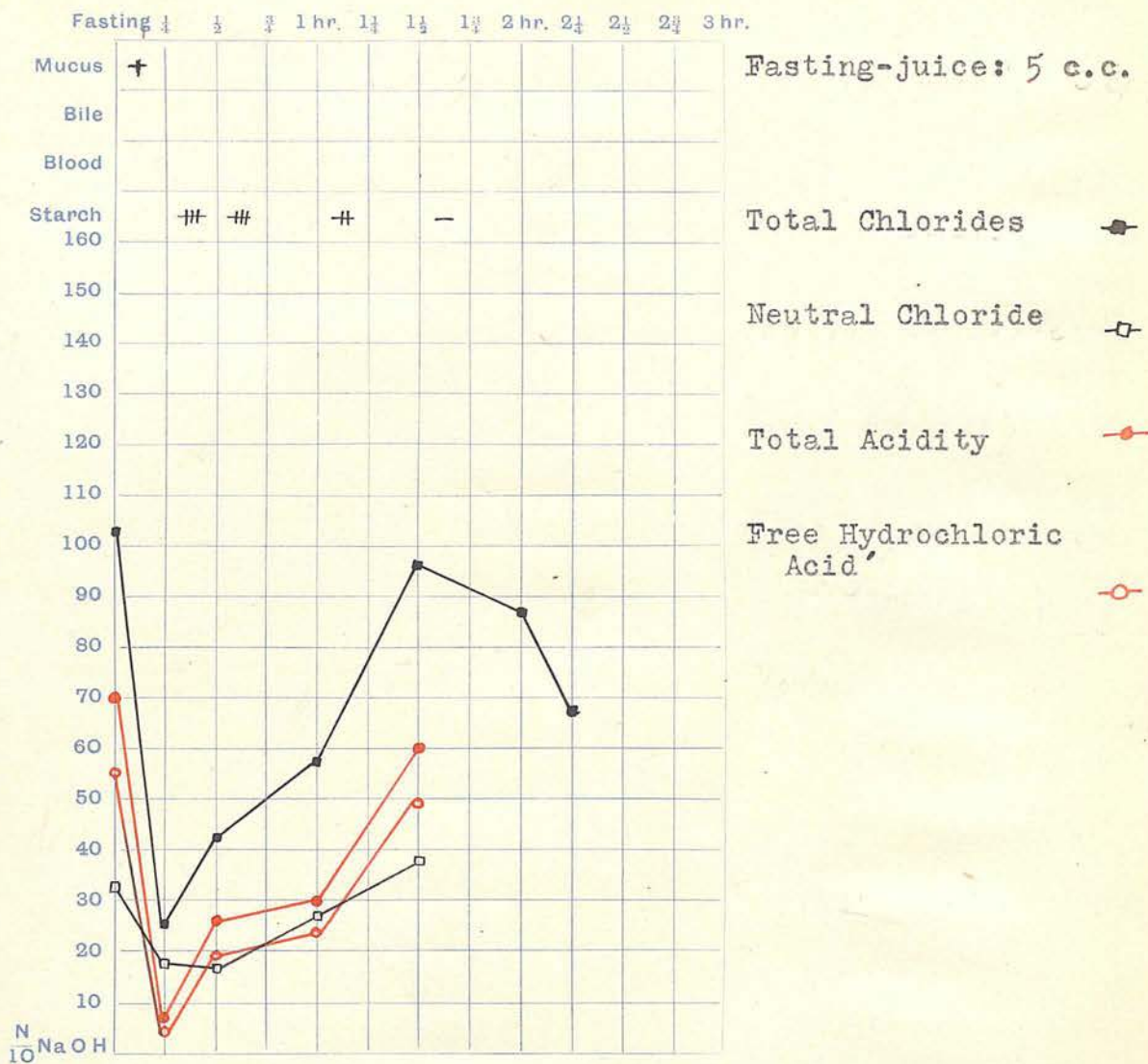
C H A R T S

REPRESENTING VARIATIONS of CHLORIDES and ACID
in Secretion obtained from 'Low' FUNDUS-POUCH.

Name of Patient

1. FRACTIONAL TEST-MEAL.

Date 6. 3. '29.



EXPERIMENTAL

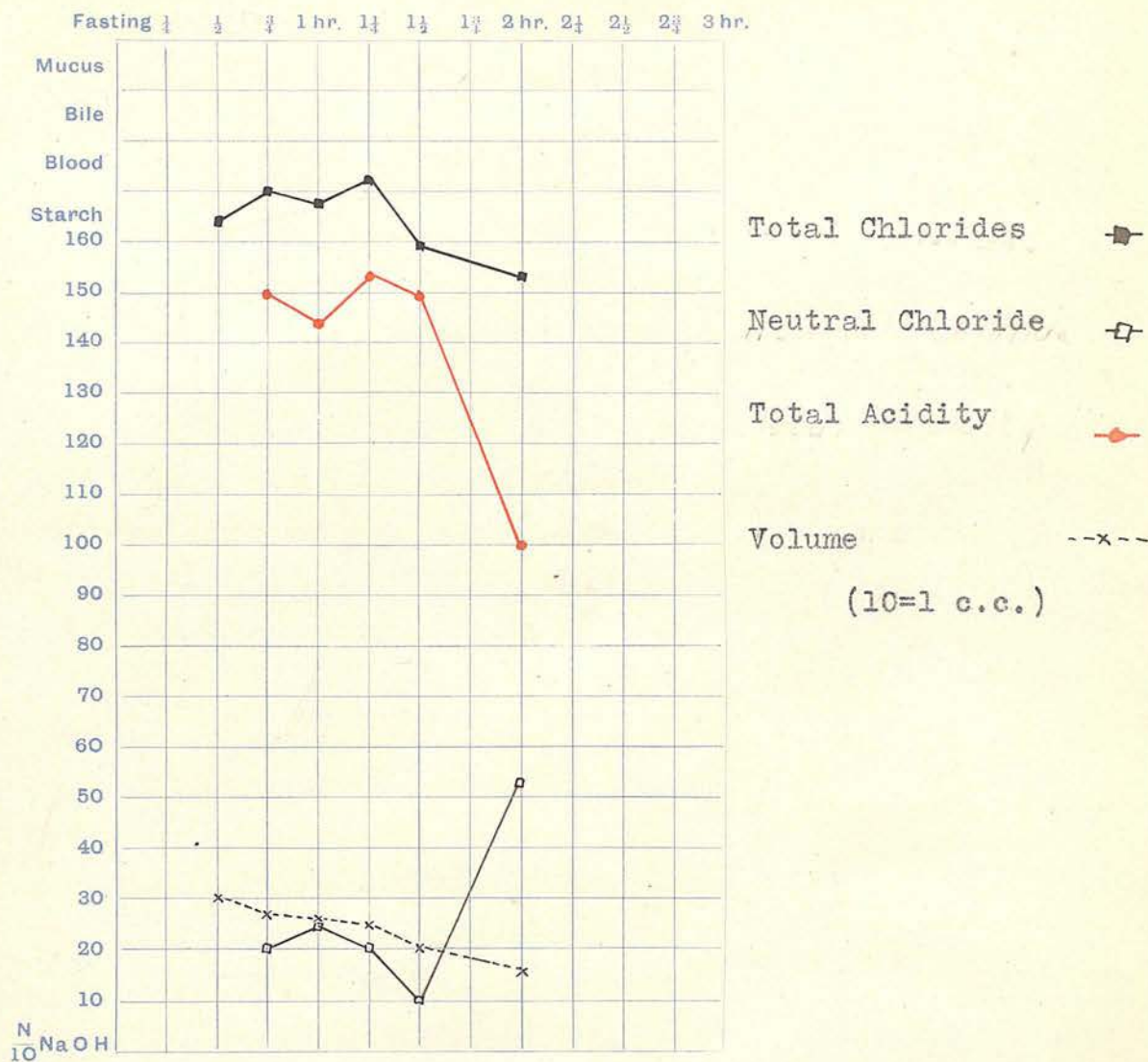
500 c.c. gruel

Specimens withdrawn by
oesophageal tube.

Name of Patient

1. FRACTIONAL TEST-MEAL.

Date 1. 6. '29.



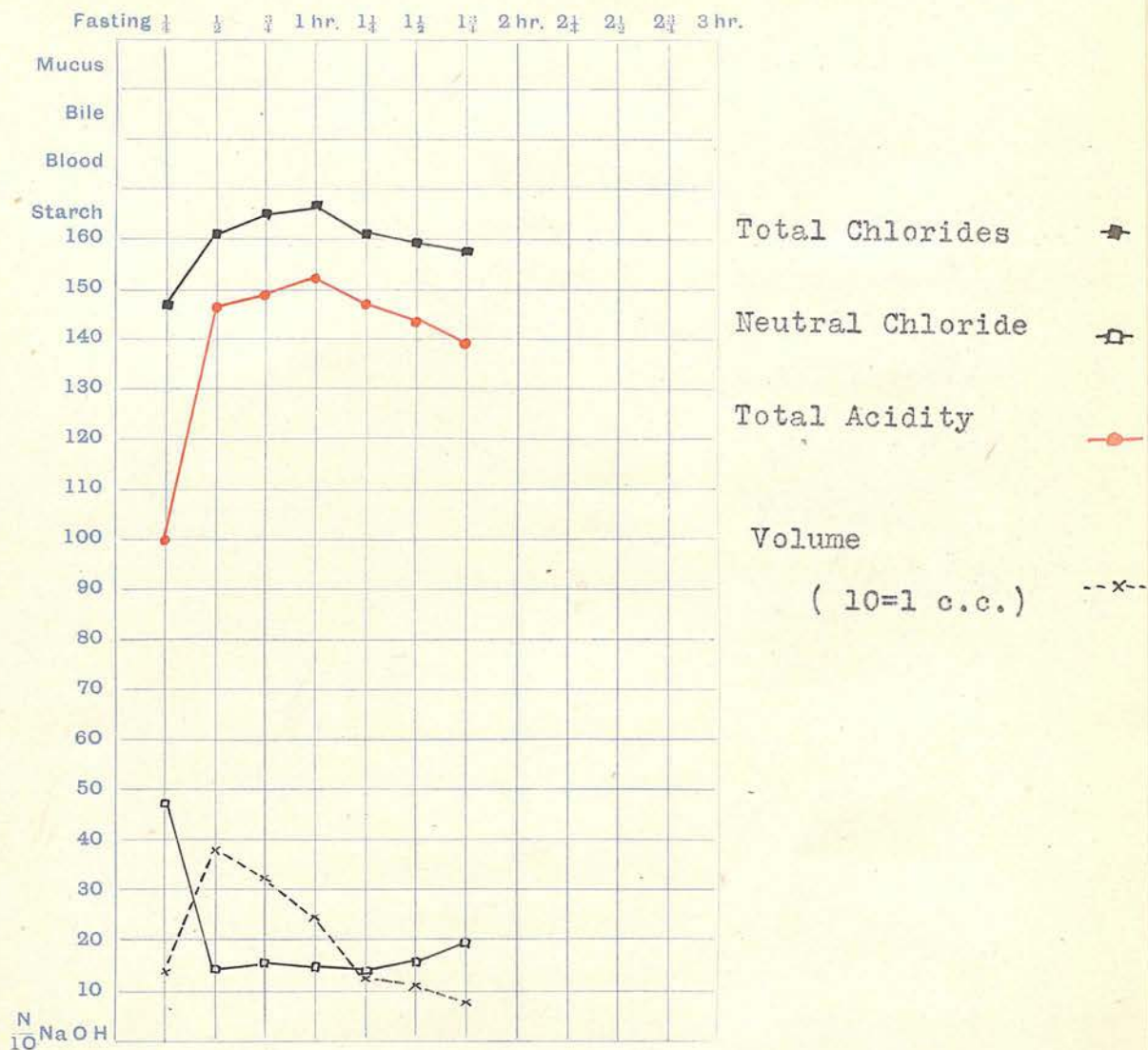
EXPERIMENTAL

100 Gm. Meat.

Name of Patient

1. FRACTIONAL TEST-MEAL.

Date 4. 6. '20.



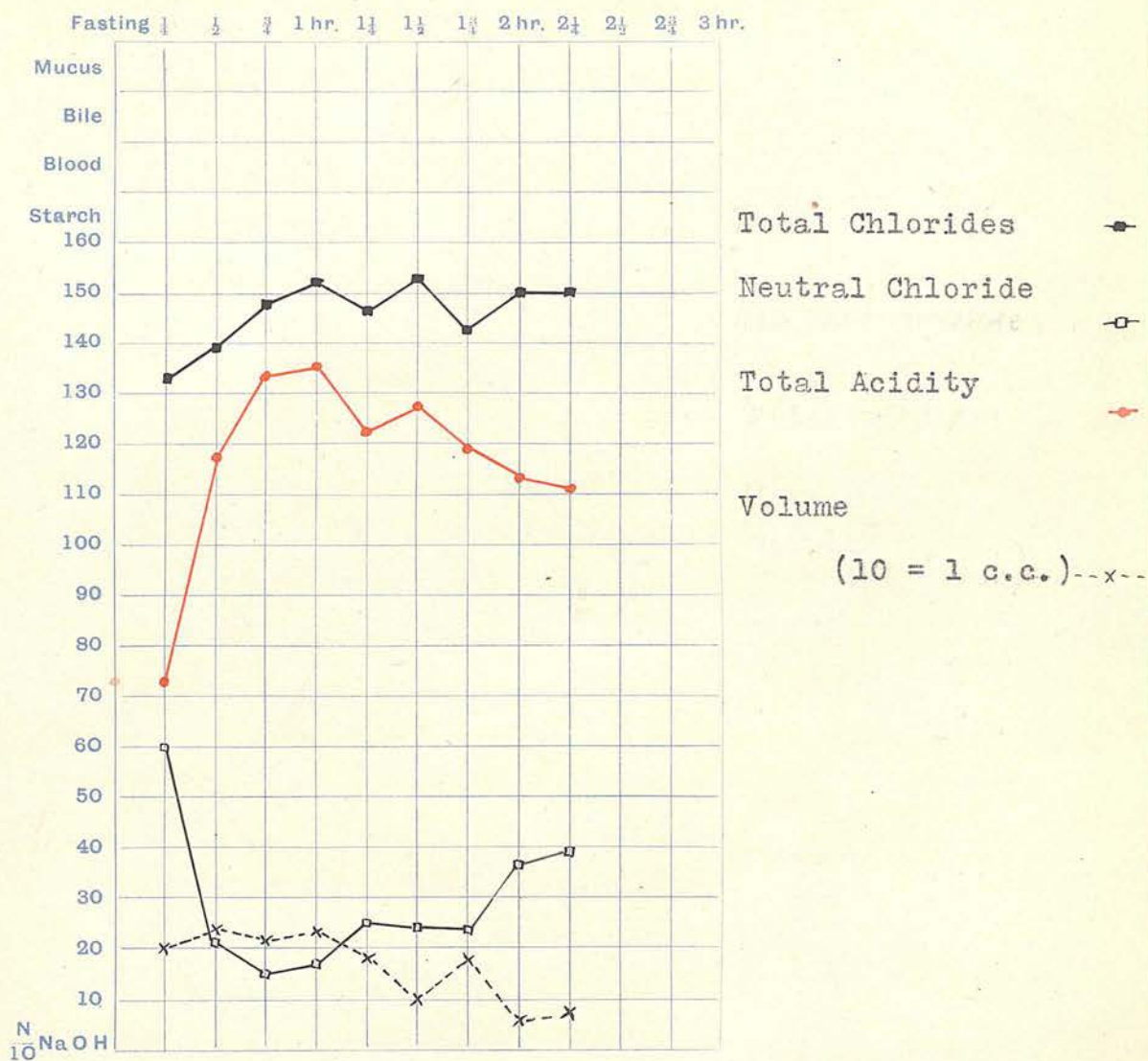
EXPERIMENTAL

300 c.c. Milk.

Name of Patient

1. FRACTIONAL TEST-MEAL.

Date 6. 6. '29.



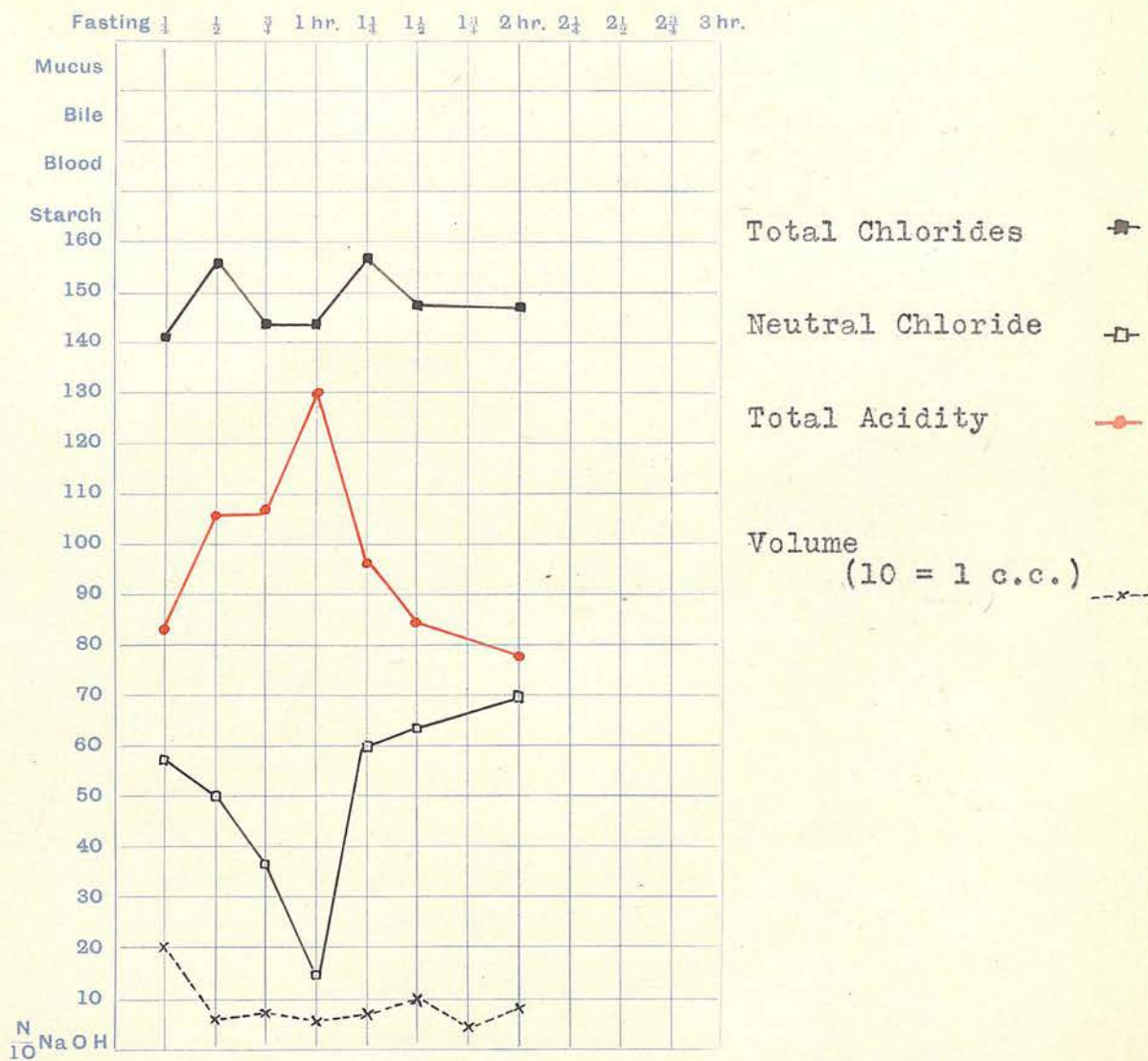
EXPERIMENTAL.

75 Gm. Dog Biscuit.

Name of Patient

1. FRACTIONAL TEST-MEAL.

Date 7. 6. '29.



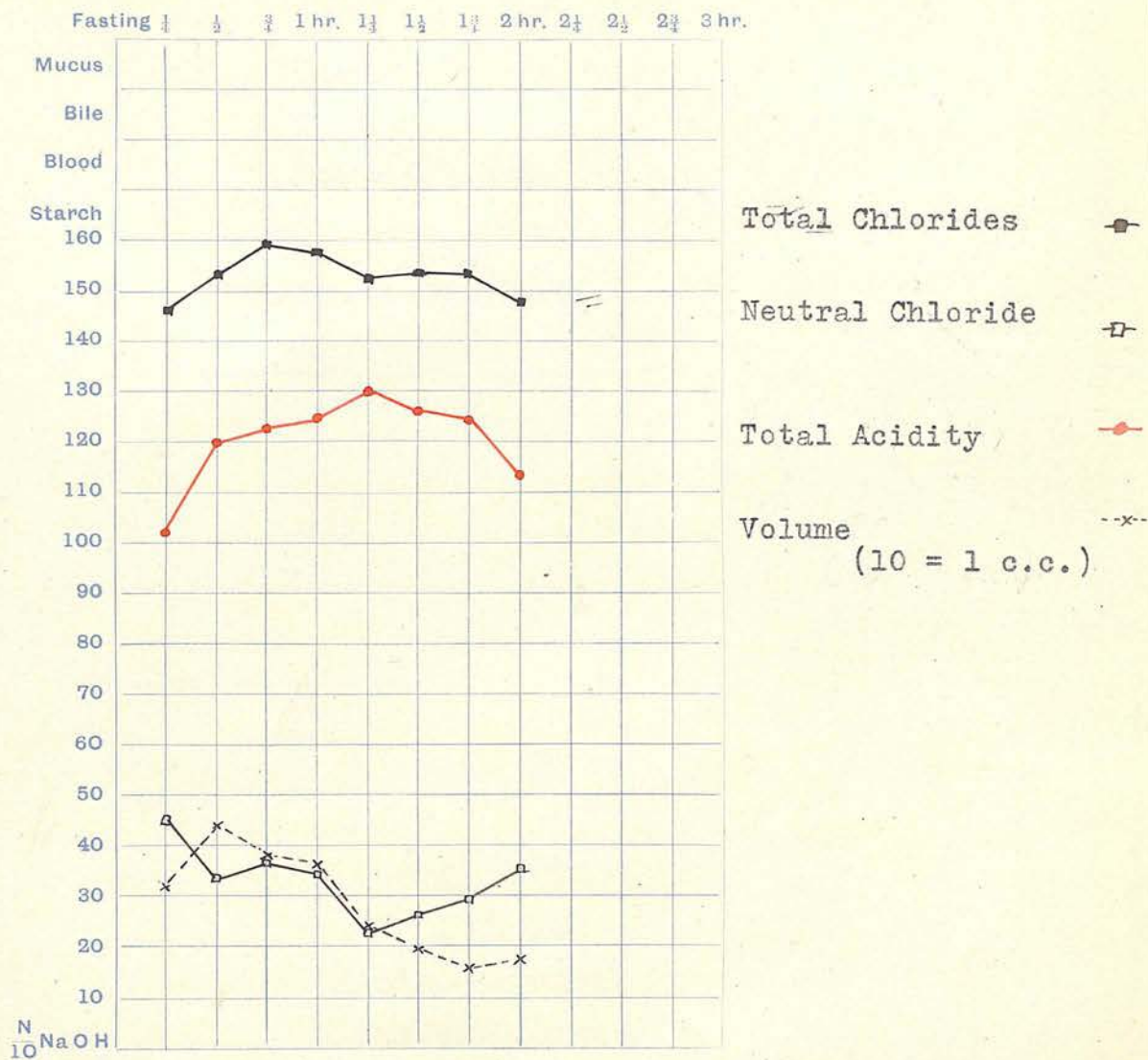
EXPERIMENTAL

300 c.c. Milk.

Name of Patient

1. FRACTIONAL TEST-MEAL.

Date 8. 6. '29.



EXPERIMENTAL

200 Gm. Equal amounts of Biscuit
Meat and Milk;

DIAGRAMS
of
OPERATIONS PERFORMED.

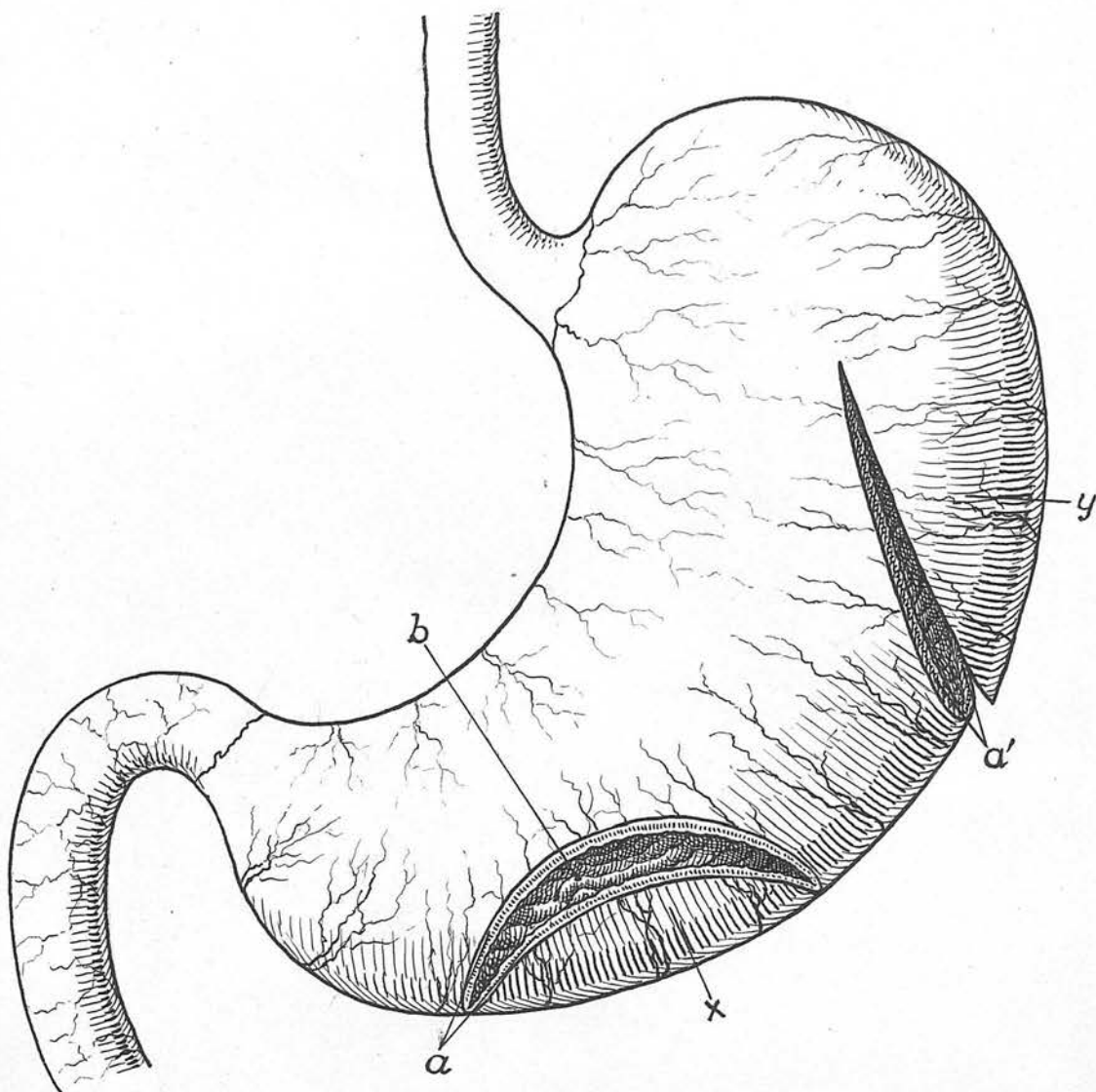


FIGURE I.

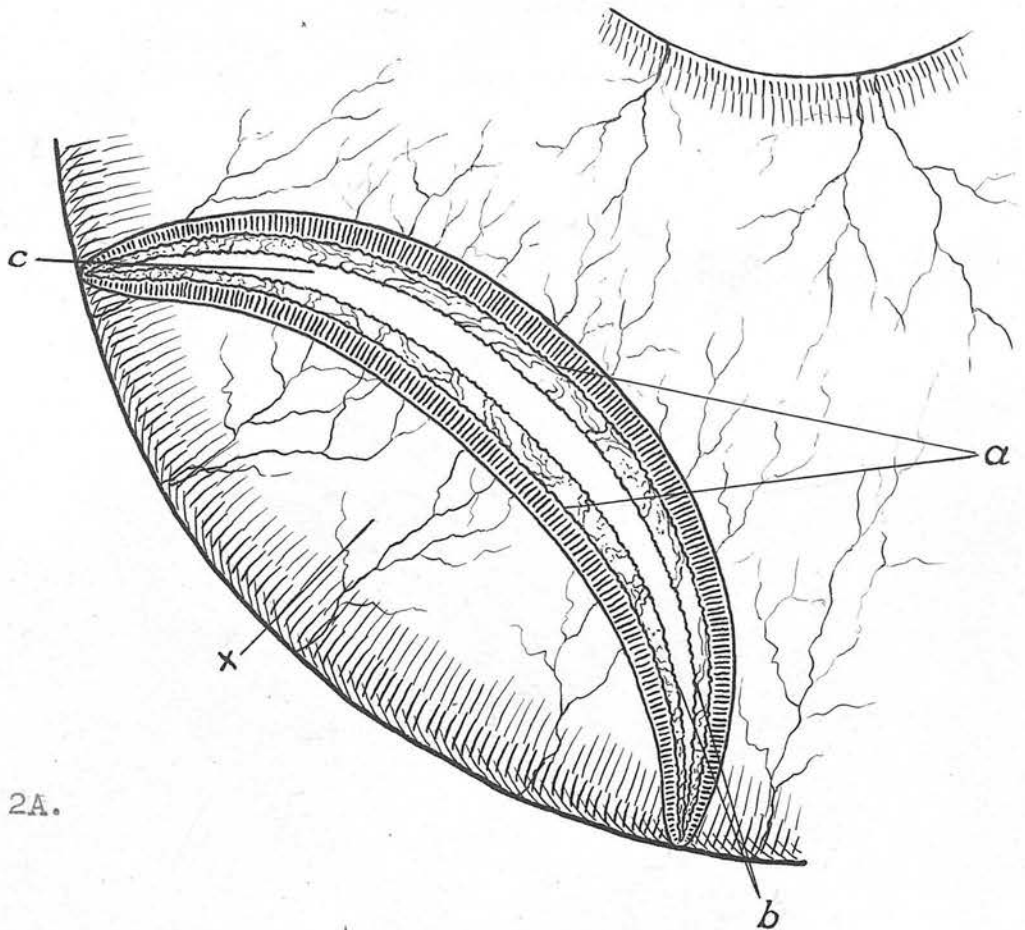
To illustrate incisions

x = 'low' fundus-pouch

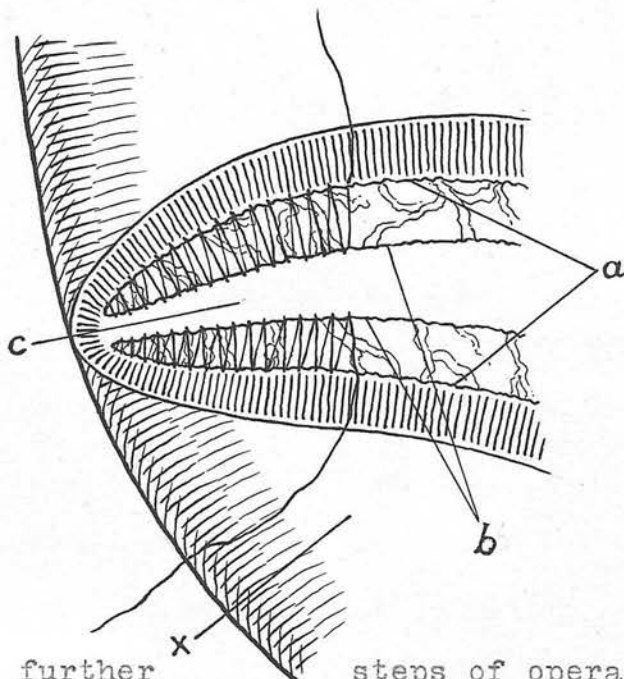
y = "Pavlov-pouch"

a, a': anterior wall of stomach

b. : mucous membrane of posterior wall.



FIGURES 2, & 2A.



To illustrate further steps of operation for 'low fundus-pouch (x).

- a. Mucous membrane of anterior wall of stomach.
- b. Mucous membrane of posterior wall of stomach incised, exposing -
- c. Submucous layer of posterior wall.

NOTE Method of suturing mucosa.

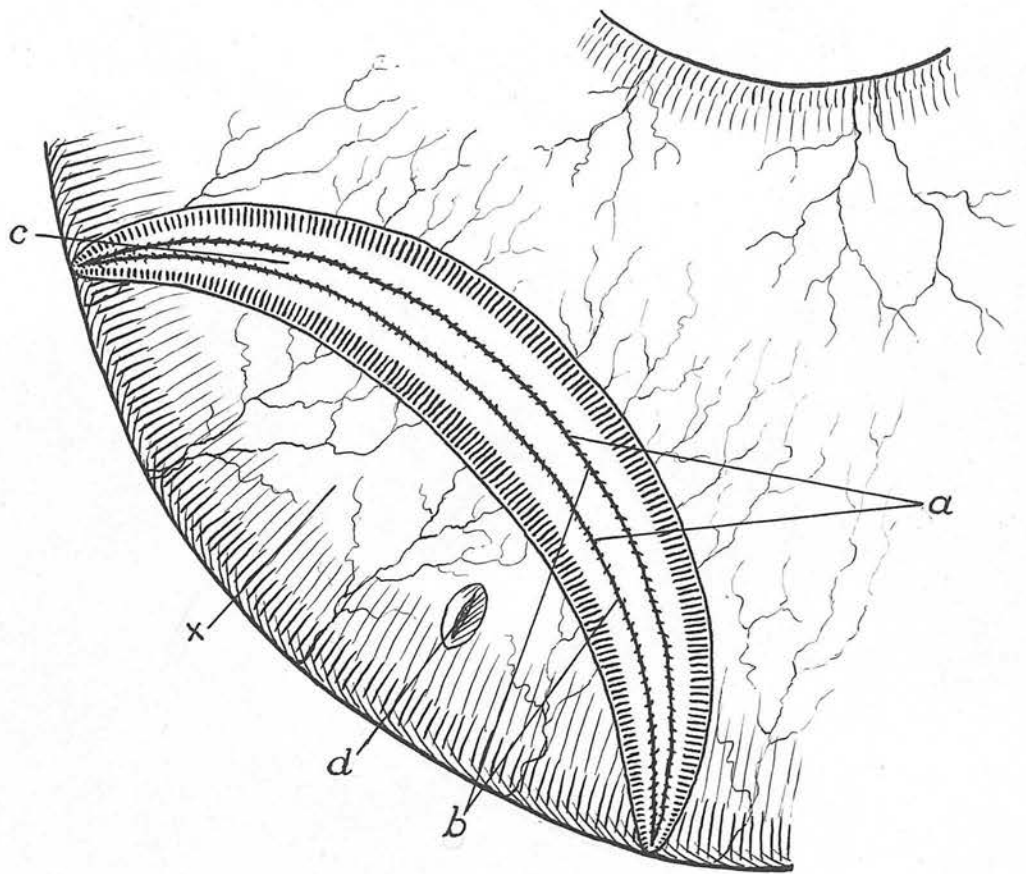


FIGURE 3.

The final stage of formation of 'low' fundus-pouch.
Cavities of pouch and stomach proper separated by
double reflection of mucosa.

x, a, b and c, as before.

d, aperture for insertion of catheter.

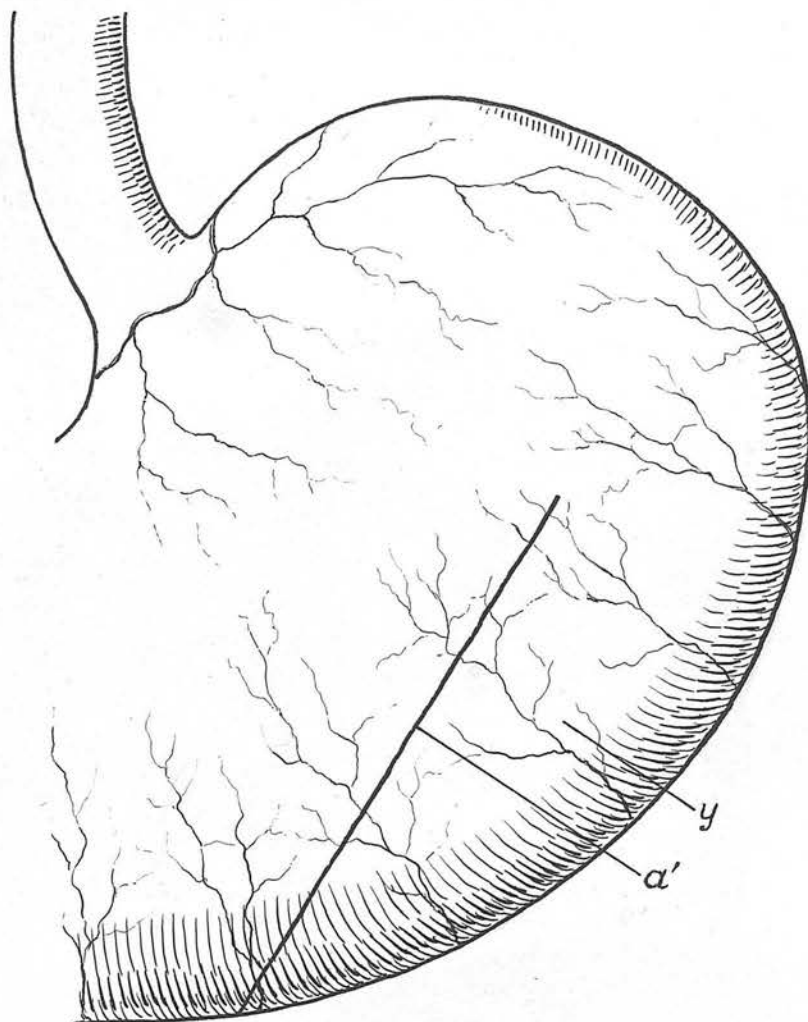
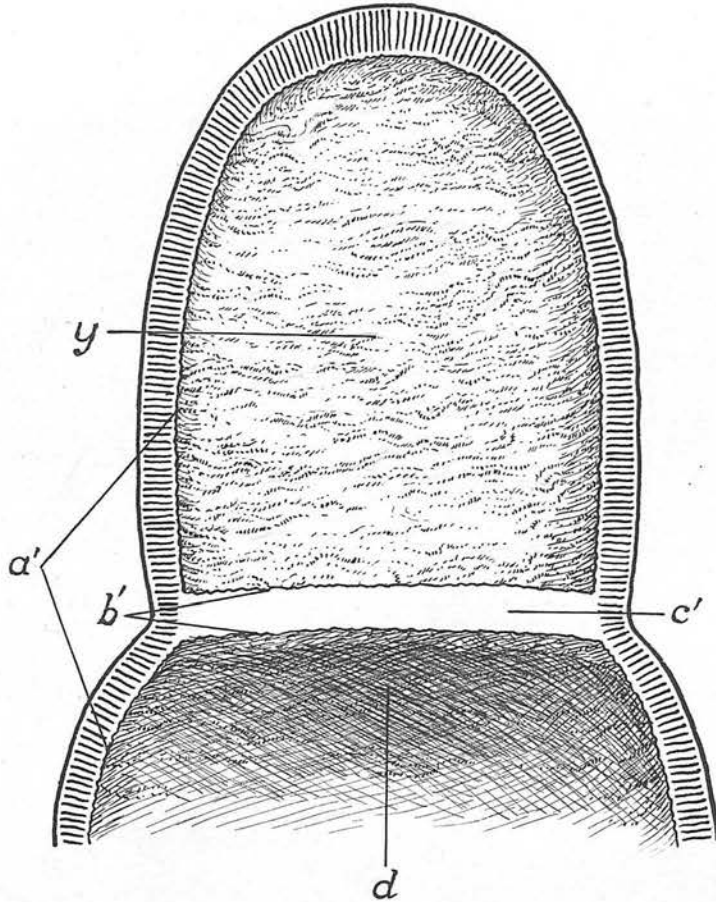


FIGURE 4.

To illustrate incision for 'Pavlov-pouch'.

y = portion of stomach destined to form pouch.

FIGURE 5.



Flap opened out and viewed from caudal aspect.

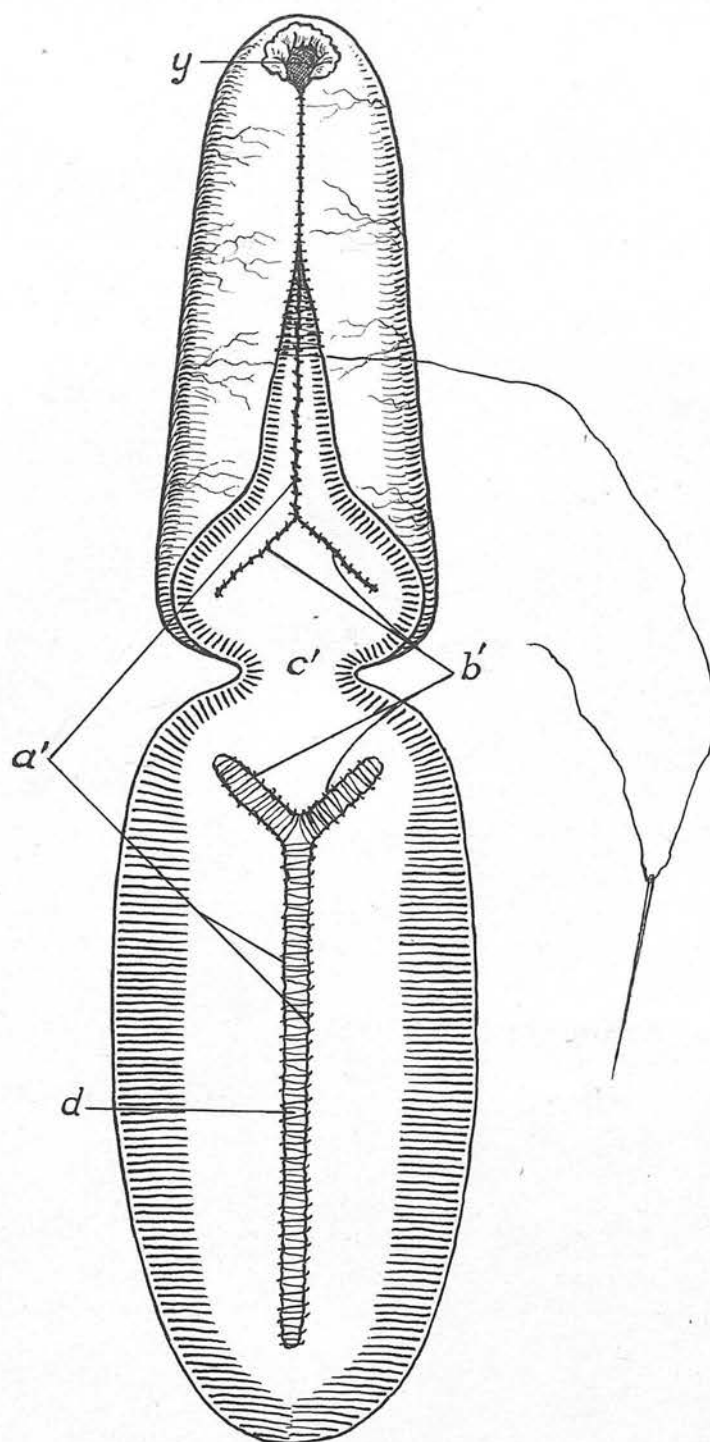
y = mucous membrane of flap.

a' = mucous membrane divided by first incision.

b' = mucous membrane at base of flap divided by
second incision, exposing -

c' = submucous layer of base of flap.

FIGURE 6.



Illustrating formation of 'Pavlov-pouch'.

- d. = Cavity of stomach-proper
- y. = Aperture of 'Pavlov-pouch'.
- a' = Mucous membrane of anterior and posterior walls of stomach included in first incision.
- b' = Mucous membrane at base of flap, divided by second incision.
- c' = Submucous layer of base of flap.

PHOTOGRAPHS OF

- (a) Apparatus Employed in Experimental Work and
 - (b) Specimens obtained.
-

P L A T E I.

METHOD of supporting animal
during collection of
Secretion from Gastric Pouch.

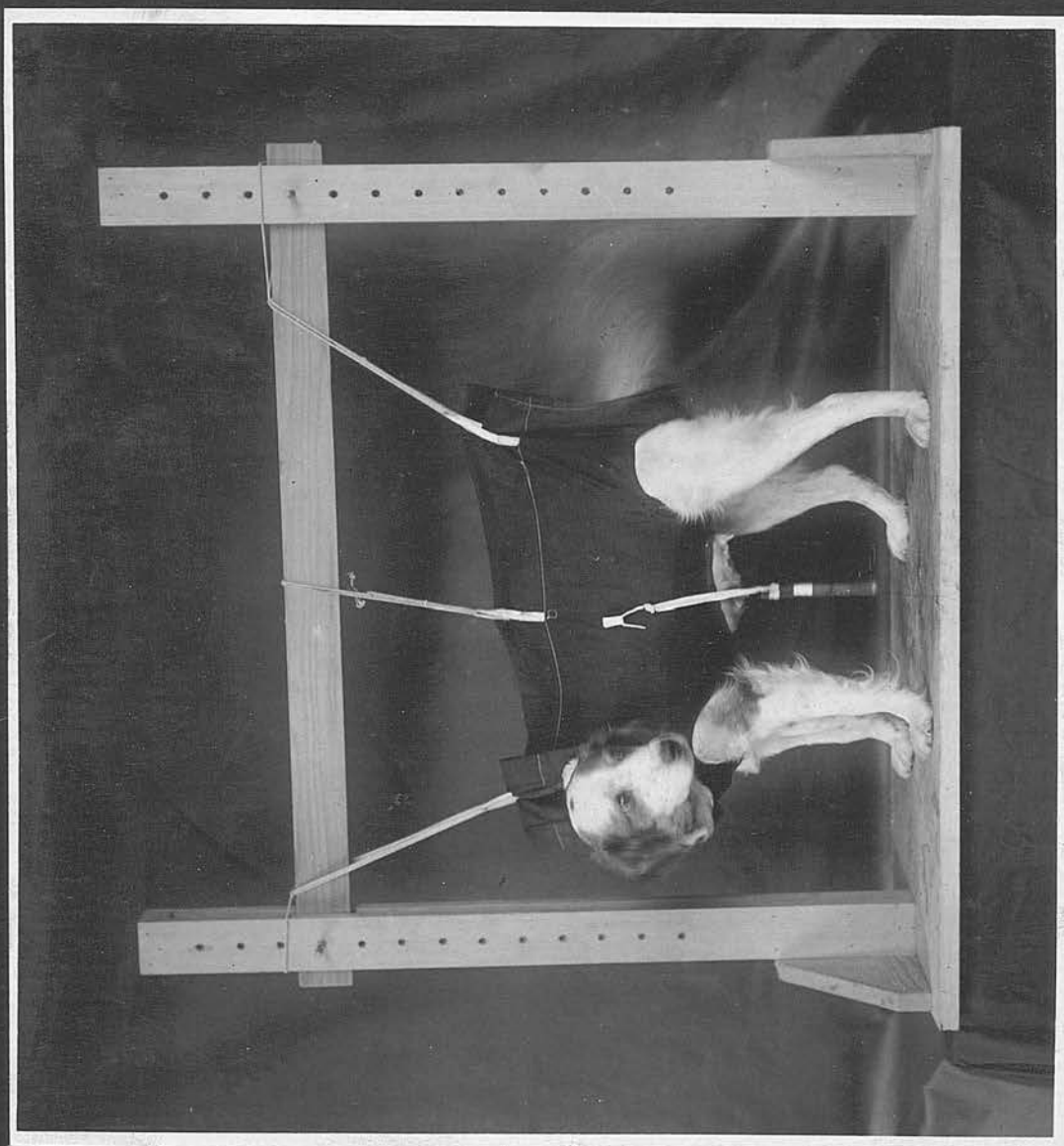


PLATE II.

To show arrangement of CATHETER and
COLLECTING-TUBE.



PLATE III.

LEFT: Portion of abdominal wall to show relative positions of outlets from Gastric Pouches.

NOTE catheter in situ in 'low' fundus-pouch and recent left paramesial incision.

RIGHT: Whole stomach after removal.

NOTE catheter inserted in 'low' fundus-pouch, also recently formed Pavlov-pouch.

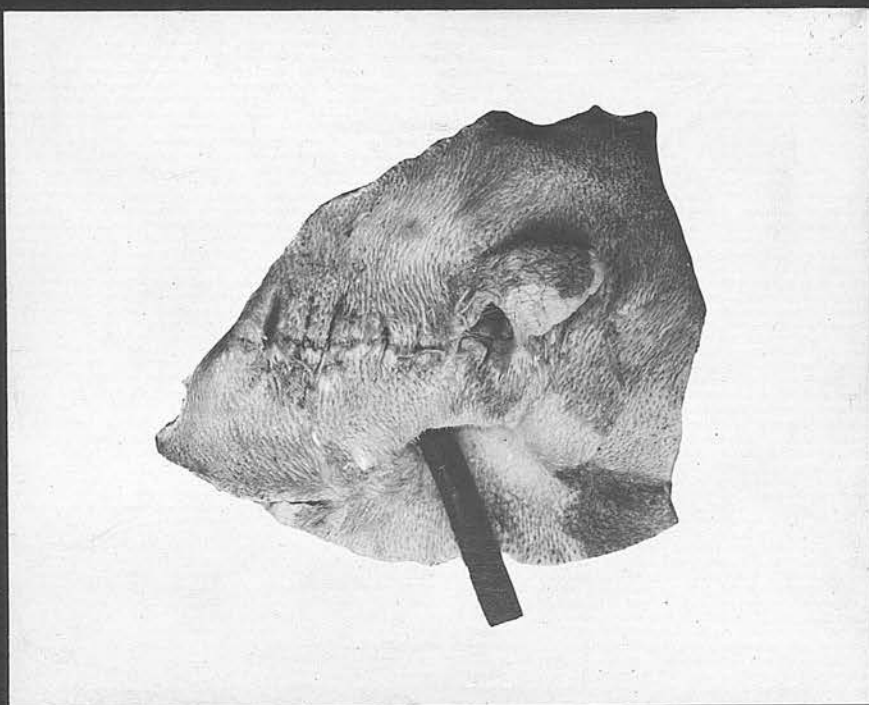
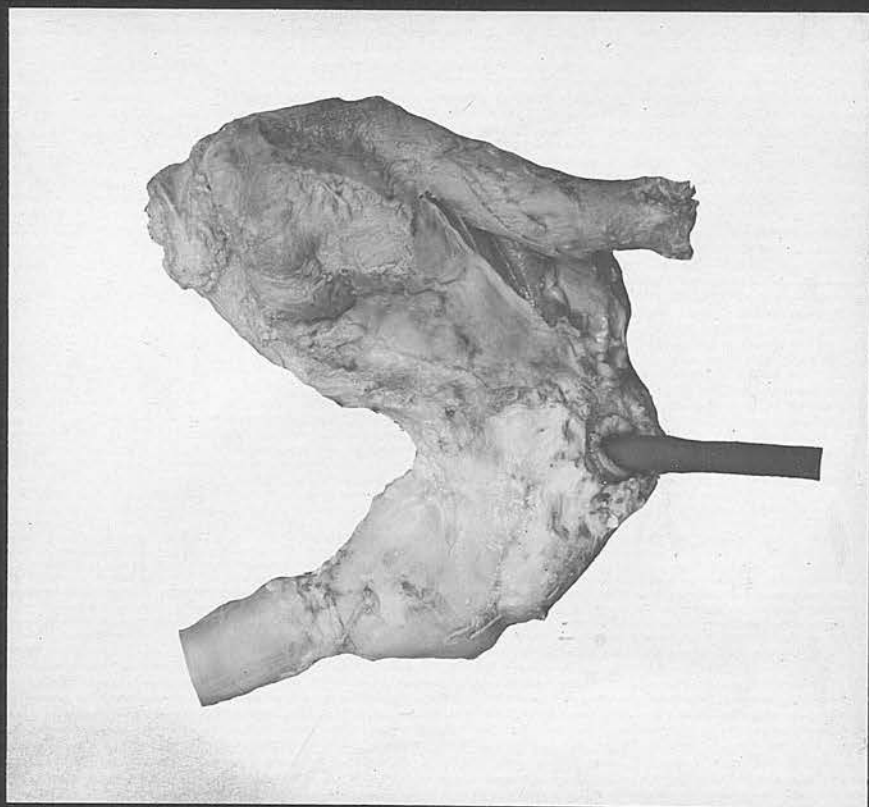
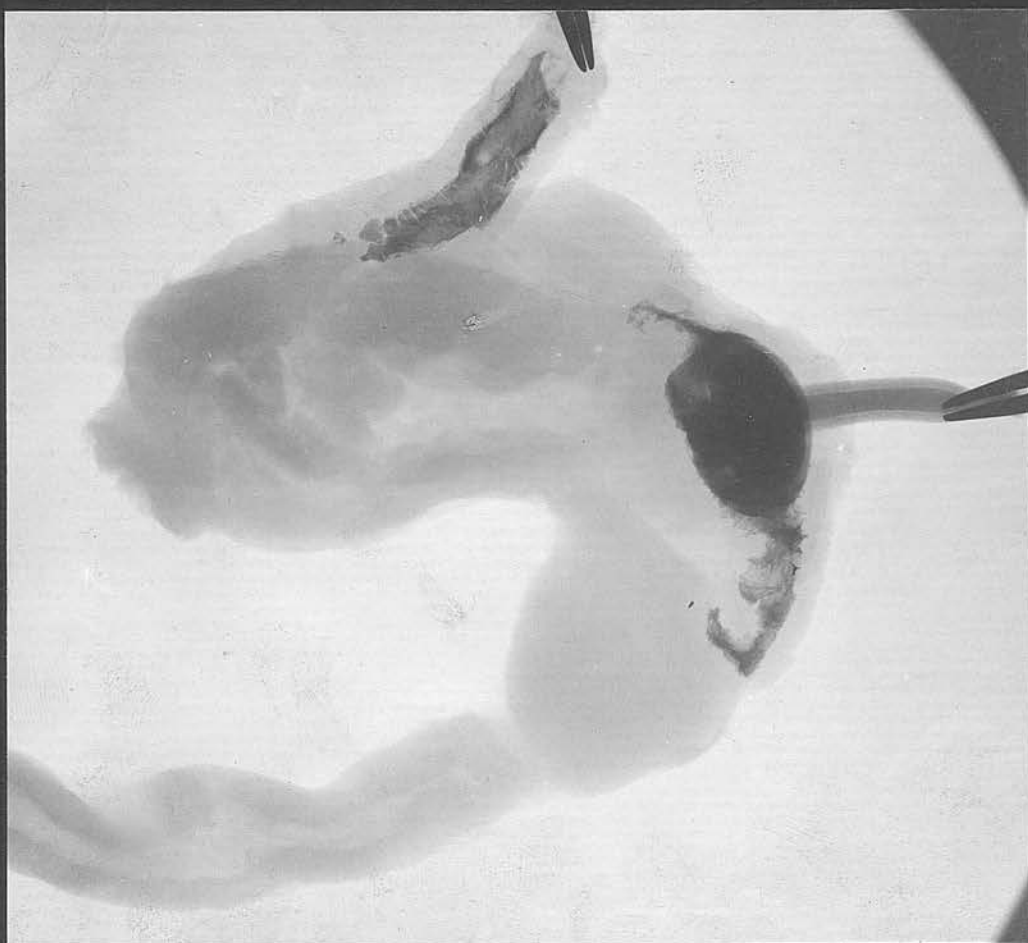


PLATE IV.

LEFT: Skiagram showing pouches injected with
barium emulsion under pressure.

RIGHT: Section of whole stomach, showing
positions of two pouches and
disposition of the mucous membrane.



P L A T E V .

UPPER left; (High power) - Transverse section of
mucous membrane of lower pouch.

NOTE parietal cells darkly stained at
periphery of acini.

LOWER left; (High power) - Longitudinal section
of mucous membrane of lower pouch. 'Parietal'
cells again shown.

RIGHT ; (Low power) - Section showing
juxtaposition of mucosa of stomach proper
(above) and 'low' fundus-pouch (below).
Apparent incompleteness of mucous membrane
due to uneven shrinkage of specimen during
fixation-process.

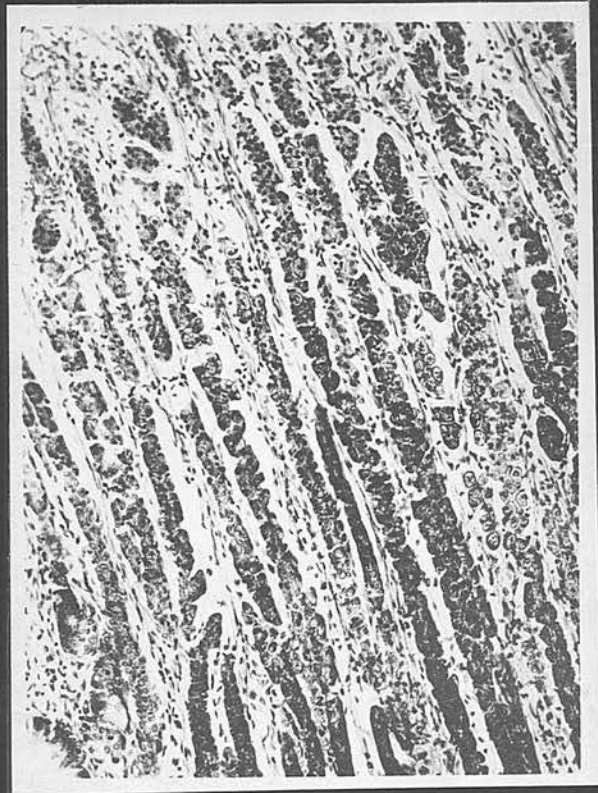
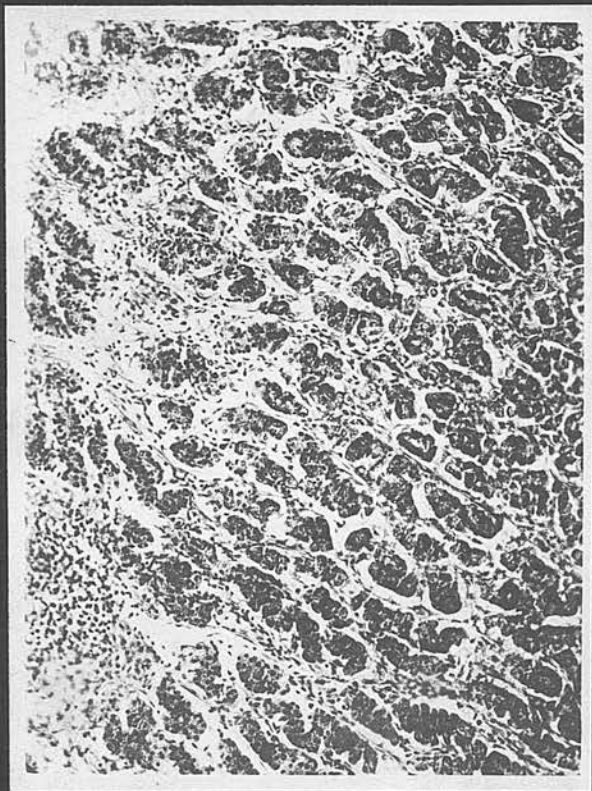


PLATE VI.

LEFT: (Low power) - Axial section to show
pyloric mucosa.

RIGHT: (Low power) - To show relation of mucous
membrane of stomach proper and Pavlov-
pouch respectively.

